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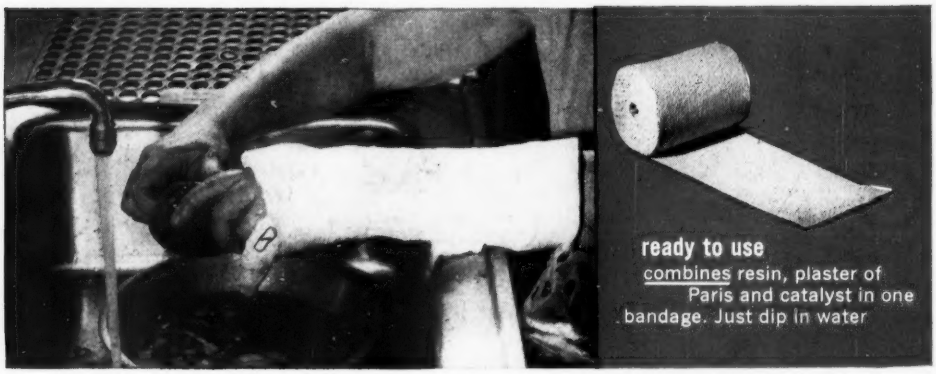

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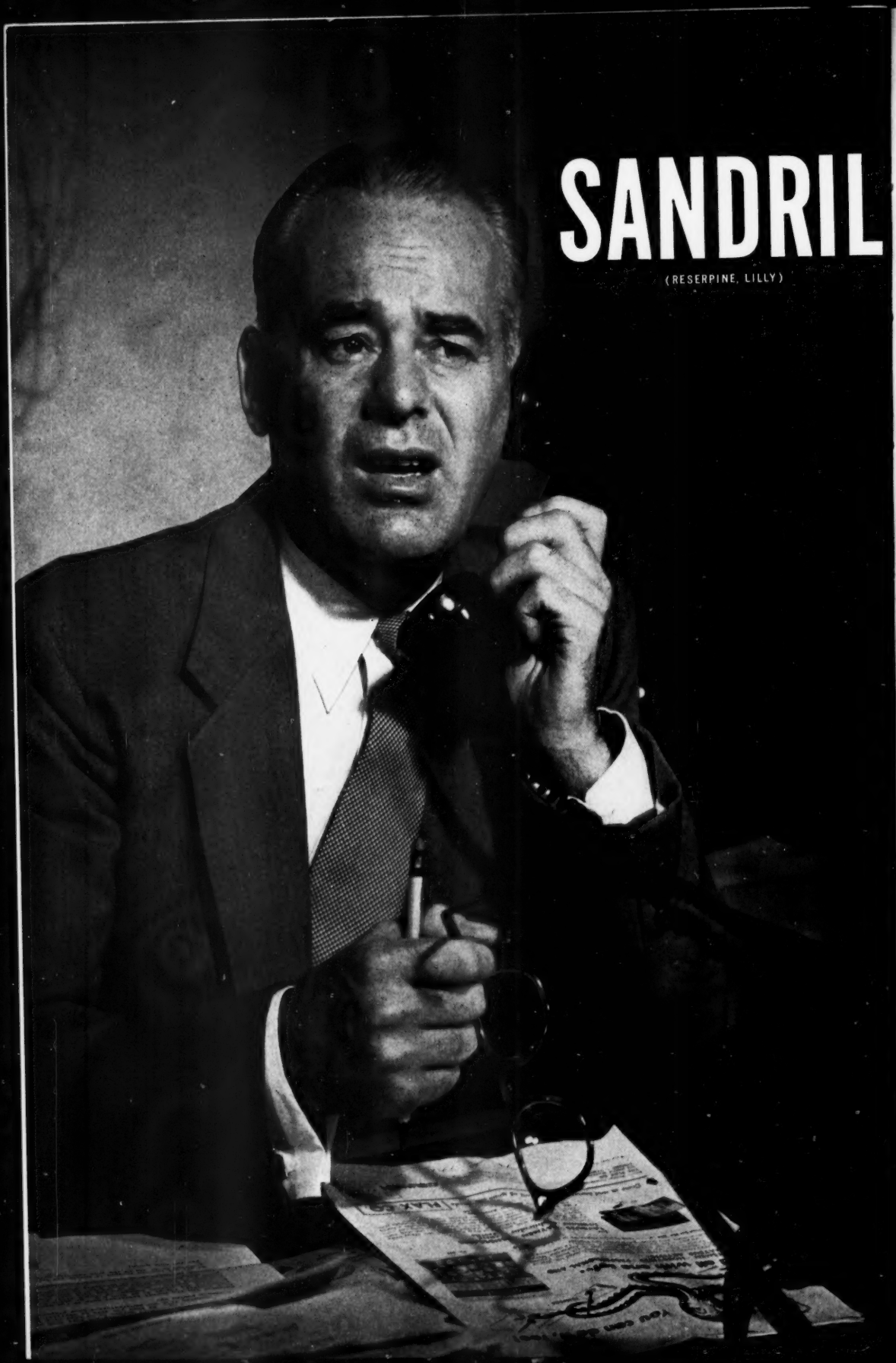
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VOLUME 99 OCTOBER, 1954 NUMBER 4

THE PATHOGENESIS OF ASCITES AND A CONSIDERATION OF ITS TREATMENT

JOHN L. MADDEN, M.D., F.A.C.S., JOHN M. LORÉ, JR., M.D.,
FRANK P. GEROLD, M.D., and JACOB M. RAVID, M.D., New York, New York

THE pathogenesis of ascites is a perplexing problem relative to which there is no unanimity of opinion. Although many postulates have been proposed, none has approached the ideal of demonstrating a common basic factor for the formation of ascites regardless of the disease process with which it is associated.

In cirrhosis of the liver the concept that has been most generally accepted is that the ascites is due to a progressive intrahepatic fibrotic obliteration of the portal vascular bed. The first to cast doubt on this concept was Herrick in 1907. This investigator, using solutions of normal saline, perfused fresh cadaver specimens of the normal liver and the liver with cirrhosis and showed that gram for gram of liver substance, a greater volume of fluid was used in the perfusion of the portal vascular bed in the liver with cirrhosis than in the normal liver. Although Eppinger confirmed these studies, McIndoe was unable to duplicate them. In addition to the perfusion experiments, McIndoe injected specimens of the normal liver and the liver with cirrhosis using varying colored solutions of celloidin. The parenchyma was digested with commercial hydrochloric acid (30 per cent) and the resulting casts of the intrahepatic circulation were studied. McIndoe concluded that in cirrhosis of the liver there was a deficit in all of the intrahepatic vascular systems, the deficit being most pronounced in the portal and hepatic venous beds. The degree of the deficit

From the Surgical Research Laboratory and the Departments of Surgery and Pathology, St. Clare's Hospital, New York, N.Y.

Fig. 1. Corrosion specimen of the whole of the normal liver, showing the uniformity in the pattern of the intrahepatic circulation.

Fig. 2. Corrosion specimen of a portion of the normal liver to show the close relation between the branches of the hepatic artery (red) and the tributaries of the portal vein (yellow).

Fig. 3. Corrosion specimen of the liver with cirrhosis and irreversible ascites. The extensive obliterative fibrosis of the common outflow tract, the hepatic veins (blue), and the compensatory increase in the vascular bed of the inflow tracts, the portal vein (yellow), and the hepatic artery (red), may be observed.

Fig. 4. Close up view of corrosion specimen of the liver with cirrhosis and irreversible ascites to demonstrate the marked disproportion (reciprocal pattern) in the vascular bed of the inflow and outflow tracts.

Fig. 5. Comparative study of the intrahepatic portal (yellow) and hepatic (blue) venous beds. Left, The reciprocal pattern relationship in cirrhosis of the liver with irreversible ascites characterized by an obliterative fibrosis of the outflow tract, the hepatic veins (blue) and a compensatory and absolute increase in the inflow tract, the portal vascular bed (yellow). Center, The uniformity of the vascular pattern in the normal liver. Right, The symmetrical pattern in cirrhosis of the liver without ascites or with ascites of the reversible (functional) type, characterized by a symmetrical deficit in both the portal and hepatic venous beds.

Fig. 6. Corrosion specimen of cirrhosis of the liver without ascites showing the symmetrical deficit in the intrahepatic portal (yellow) and hepatic (blue) venous beds. The adequacy of the outflow tract, the hepatic veins (blue), is evident.

was believed to vary in direct ratio to the severity of the disease process.

In 1942, Dock, using kerosene, repeated the perfusion studies of Herrick and McIndoe. In cirrhosis of the liver, a diminution in the total volume of perfusion fluid, hepatic arterial and portal venous, was observed. However, in some specimens of chronic alcoholic cirrhosis the volume of perfusion fluid in the hepatic arterial bed was increased. Furthermore, in 2 such specimens the portal bed was normal. From this study, which tended to corroborate both Herrick and McIndoe, Dock concluded that the phenomena noted by Herrick were genuine but were not applicable in all cases of cirrhosis of the liver.

In conditions other than cirrhosis of the liver, such as chronic constrictive pericarditis and congestive heart failure, ascites may be a prominent symptom. Lower, in 1728, was the first to produce ascites experimentally by ligating the thoracic segment of the inferior vena cava. In 1909, Bolton in England and Whipple and Sperry in the United States, repeated the experiments of Lower and demonstrated that if the diameter of the thoracic segment of the inferior vena cava was occluded partially, by either a ligature or a metallic band, ascites occurred within 24 to 36 hours. Confirmation of this study has been repeatedly obtained. On the contrary, complete occlusion of the abdominal segment of the inferior vena cava is not associated with ascites. Furthermore, Child and associates have shown both in the experimental animal, the Macaca mulatta monkey, and in the human that the portal vein may be occluded completely at the porta hepatis with survival and without the occurrence of ascites. Furthermore, it is a well established clinical observation that in patients with complete intrahepatic thrombotic obliteration of the portal vascular bed, either suppurative or nonsuppurative, ascites is absent. However, in the Budd-Chiari syndrome, characterized by a selective thrombotic occlusion of the hepatic (systemic) veins within the liver, ascites is present. The ascites is acute and a prominent clinical manifestation.

From these observations, both experimental and clinical, it was postulated that the primary factor in the pathogenesis of ascites was a blockage not of the inflow tract, the portal venous bed, but of the outflow tract, the hepatic (systemic) veins. To confirm the logic of this postulate, a comparative study of the pattern of the intrahepatic circulation in the normal liver and in the diseased liver, both with and without ascites, was undertaken. The results of this study are herein presented.

METHOD AND MATERIAL

The intrahepatic circulation in the normal liver and in the diseased liver with and without ascites was studied by the injection of varied colored solutions of neoprene latex type 571 and corrosion of the liver parenchyma with commercial hydrochloric acid (30 per cent). A yellow colored solution was used in the portal vein, red in the hepatic artery, and blue in the hepatic (systemic) veins. In this study, whole specimens of the liver from 23 fresh cadavers were injected and corroded. In 3 specimens the liver was normal and in 20 specimens it was diseased. In 14 of the diseased specimens cirrhosis of the liver was present. In 10 of these, absent irreversible ascites was present clinically and in the other 4.

In 3 specimens there were extensive liver metastases. In 2 the metastases were secondary to a primary bronchogenic carcinoma, in 1 of which ascites was an associated clinical manifestation. In the remaining specimen the primary lesion was a carcinoma of the breast. There was no associated ascites. In each instance the livers were huge and weighed 4,500, 4,300, and 4,600 grams respectively.

In 3 specimens congestive hepatomegaly secondary to congestive heart failure was present. Clinically, in 2 of these there was ascites. In 1 of the 2 with ascites there was an associated anasarca. Although in this patient the liver was palpable at the level of the pelvic brim, it weighed only 1,280 grams. This disparity in the antemortem size of the liver and its weight postmortem demonstrates well the elasticity and distensibility of the liver framework.

OBSERVATIONS

In the 3 specimens of the normal liver a uniformity in the pattern of the intrahepatic cir-

culation was observed (Fig. 1). The tributaries of the portal and hepatic veins and the branches of the hepatic artery appeared in constant equilibrium. The hepatic artery and its branches were closely related to the portal vein and its tributaries (Fig. 2). The hepatic veins, though they appeared as isolated areas of blue, were uniform in their distribution throughout the liver and constant in their relation to the branches of the hepatic artery and the tributaries of the portal vein (Fig. 1). Intrahepatic communications between the portal vein (yellow) and the hepatic veins (blue) were depicted by the appearance of a chartreuse color which indicated an admixture of the two primary colors: yellow (portal system) and blue (hepatic veins). There were no intrahepatic demonstrable communications between the hepatic artery and the portal vein or the hepatic artery and the hepatic veins.

In cirrhosis of the liver the pattern of the intrahepatic circulation was observed to be dependent upon the presence or absence of ascites and whether or not the ascites was reversible or irreversible. In cirrhosis of the liver with irreversible ascites there was a reciprocal pattern of the circulation within the liver characterized by an absolute and compensatory increase in both the portal venous and the hepatic arterial beds, the inflow tracts, and a concomitant and absolute decrease in the hepatic (systemic) venous bed, the outflow tract (Figs. 3, 4, and 5). Contrariwise, in cirrhosis of the liver without ascites, or with ascites that was acute and reversible, there was a symmetrical pattern characterized by a symmetrical deficit in all of the vascular systems but most pronounced in the hepatic systemic and portal venous beds (Figs. 5 and 6). These observations relative to the gross digested specimens were confirmed by a study of the related histopathologic changes. Characteristically, in cirrhosis of the liver with irreversible ascites there was a marked increase in the size of the portal vascular bed and a concomitant decrease in the number of the central or hepatic veins (reciprocal pattern), the majority of which were occluded by an obliterative fibrosis (Fig. 7). In cirrhosis of the liver without ascites, or with ascites of the acute but reversible type, there was a diminution in both the number and size of the portal and central veins (symmetrical pattern). However, obliterative fibrosis of the central veins, though present (Fig. 8), was not as extensive as in cirrhosis of the liver with irreversible ascites. Accordingly, from the character of the histopathologic changes that occur in cirrhosis of the liver, one may state with a reasonable degree of accuracy the presence or absence of ascites as an associated clinical manifestation and whether or not the ascites is intractable (irreversible).

In the 3 liver specimens with extensive metastases, both with and without ascites, the one characteristic finding in the anatomic pattern of the intrahepatic circulation was an increase in the arterial vascular bed (Fig. 9). The relation of ascites to liver metastases is commented upon later.

In the 3 specimens of congestive hepatomegaly, 2 with and 1 without ascites, there was a distinctive pattern of intrahepatic circulation characterized by a marked increase in both the diameter and the surface area of the hepatic (systemic) veins, the outflow tract (Fig. 10). There were no concomitant characteristic changes evident in the inflow tracts, namely, the portal venous and hepatic arterial beds.

COMMENT

From the study of the anatomic pattern of the intrahepatic circulation in the normal and in the diseased human liver certain postulates relative to the pathogenesis and the treatment of ascites secondary to cirrhosis of the liver may be presented. It is postulated that the pathogenesis of ascites in cirrhosis of the liver is an obstruction of the outflow tract, the hepatic (systemic) venous bed. Independently, McFadzean of the University of Hong Kong postulated "... an obstructive element must be present in the hepatic veins."

In chronic, irreversible ascites the cause of the obstruction is believed to be an obliterative fibrosis of the hepatic veins. This is an organic occlusion that is refractory to all of the generally accepted methods of treatment. Contrariwise, in acute, temporary, or reversible ascites, the obstruction of the outflow

tract (hepatic veins) is believed due to a diffuse intrahepatic cellular edema secondary to both protein and electrolyte imbalances. In such instances the obstruction is functional and with proper diet and medication there is a restoration of the body proteins and electrolytes toward the normal. When this occurs the intrahepatic cellular edema subsides, the obstruction of the outflow tract (hepatic veins) is released, and the congestive hepatomegaly and the ascites disappear. This postulate would conform with the clinical observation of the poor prognosis in patients with cirrhosis of the liver and ascites in whom the liver is small and contracted (obliterative fibrosis of the outflow tract) and the more favorable prognosis in patients with cirrhosis of the liver and ascites in whom the liver is acutely enlarged (edematous or functional obstruction of the outflow tract). It would also conform with and offer an explanation for the apparent contradictory findings of Herrick and McIndoe and tend to prove that the propositions of both were correct. In a review of the protocols of Herrick there was no mention of an associated clinical ascites in any of the specimens of the liver with cirrhosis that were perfused. Accordingly there is the possibility that the liver specimens that were perfused were those in which there was an associated ascites of the irreversible type. The absolute and compensatory increase in the intrahepatic portal vascular bed in such specimens (Figs. 3, 4, and 6) would explain why Herrick, gram for gram of liver substance, used a larger volume of fluid in perfusing the liver with cirrhosis than in the normal liver. Although clinical ascites was associated with some of the liver specimens perfused by McIndoe, its incidence, duration, and severity were not stated. Accordingly, one may assume that McIndoe may have perfused and subsequently injected and digested liver specimens in which ascites was either absent or, if present, was of the functional or reversible type. In the study of such specimens a constant observation has been the presence of an intrahepatic deficit in both the portal and the hepatic venous beds (Figs. 5 and 6). This deficit in the portal vascular bed would explain why the volume of perfusion fluid used would be less than in the normal. It is also noteworthy that the corrosion casts of such liver specimens conformed in an almost identical pattern to the corroded celloidin casts illustrated by McIndoe (Fig. 13b).

In congestive heart failure and in chronic constrictive pericarditis it is again postulated that the pathogenesis of the ascites is an obstruction of the outflow tract, the hepatic veins. The obstruction is believed due to an intrahepatic cellular edema and congestive hepatomegaly secondary to chronic venous stasis in the thoracic segment of the inferior vena cava.

In patients with extensive metastases in the liver and associated ascites the pathogenesis of the ascites is also best explained on the basis of obstruction of the hepatic veins. The obstruction may be both organic (tumor) and functional (intrahepatic cellular edema). The functional component is believed related to alterations in both body electrolytes and protein metabolism secondary to the disease process. This postulate would conform with the absence of characteristic organic changes in the gross digested specimens other than an increase in the arterial vascular bed (Fig. 9).

Fig. 7. Photomicrograph of the histopathologic pattern in cirrhosis of the liver with irreversible ascites. Characteristically there is an extensive obliterative fibrosis (organic) of the central veins (center area) and a concomitant increase in the portal vascular bed (periphery). Hematoxylin and eosin stain, low power.

Fig. 8. Photomicrograph of the histopathologic pattern in cirrhosis of the liver without ascites. The central veins, though diminished, are easily identified. There is no increase in the adjacent portal vascular bed. Hematoxylin and eosin stain, low power.

Fig. 9. The intrahepatic circulation in a specimen of the liver in which there are extensive carcinomatous metastases. Characteristically there is a pronounced increase in the hepatic arterial (red) vascular bed.

Fig. 10. Close up view of the intrahepatic circulation in congestive heart failure with ascites. The marked increase in the vascular bed of the outflow tract, the hepatic veins (blue), is evident.

Fig. 11. Corrosion specimen of a segment of the midportion of the jejunum showing extensive intramural portal varices.

Fig. 12. Injected fresh cadaver specimen, demonstrating a pre-existing portacaval shunt. The shunt vein, 4 millimeters in its narrowest diameter, extends in a horizontal plane from the venous bed in the base of the mesentery of the terminal ileum to the right ovarian vein. The passage of blood from the shunt vein to the kidney through the ovarian vein, the inferior vena cava, and the renal veins is depicted.

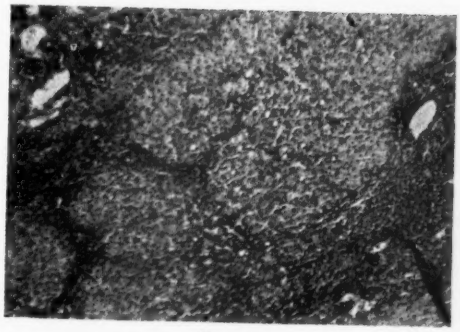
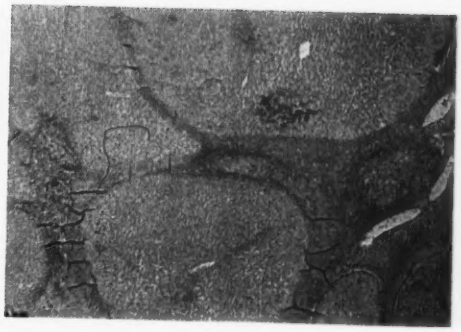


Fig. 7.



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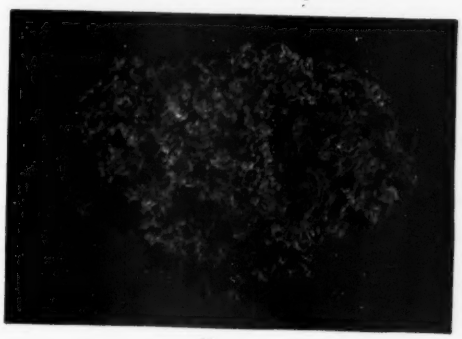

Fig. 9.

Fig. 10.

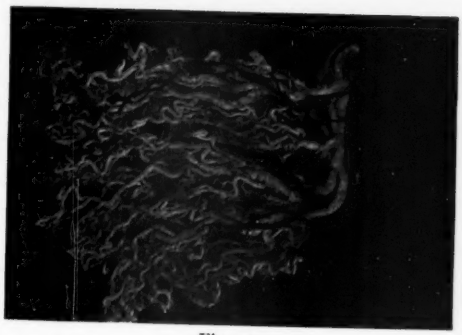

Fig. 11.

Fig. 12.

(Legends on opposite page.)

a b

Fig. 13. Illustration (courtesy of *Arch. Path.*, 1928, 5: 22–42) from McIndoe (9) showing celloidin casts of the intrahepatic venous beds, portal (black) and hepatic (white) in the, a, normal liver and, b, liver with cirrhosis. The symmetrical deficit of the venous beds in, b, is in conformity with the pattern of the intrahepatic circulation in cirrhosis of the liver without ascites (Figs. 5 and 6).

In the liver the hepatic venous bed is the common outflow tract for both the hepatic artery and the portal vein. Whenever this outflow tract is obstructed, nature, as elsewhere in the vascular system, attempts to overcome the obstruction by an increase in the available collateral bed both arterial (hepatic artery) and venous (portal vein) (Figs. 3 and 4). The problem in cirrhosis of the liver with irreversible ascites is believed to be not, as so frequently stated, one of too much blood being brought to the liver. The fact that there is an increase in the collateral vascular bed, both intrahepatic and extrahepatic, is interpreted as an expression of nature's attempt to compensate for the obstruction to the outflow tract of the liver, the hepatic veins. Accordingly, the performance of an extrahepatic portacaval shunt as a method of treatment would seem to be a compromise of nature on the venous side (portal vein). In like manner ligation of the hepatic artery would seem to be a compromise of nature on the arterial side. Furthermore, treatment by the establishment of an end-to-side arteriovenous communication between the divided and proximal end of the hepatic artery and the side of the portal vein is believed contraindicated on the theoretical basis that: (1) it does not attack the basic pathologic feature of the disease, the obstruction of the outflow tract, the hepatic veins; and (2) division of the hepatic artery is a compromise of nature on the arterial side as previously mentioned. Accordingly any of these procedures is believed interdicted. In the treatment of patients with cirrhosis of the liver and irreversible ascites, the ideal is the correction of the basic pathologic feature of the disease, the obliterative fibrosis of the outflow tract. A suggested method of treatment, used in 2 patients and called hepatopexy, is the application of magnesium trisilicate powder to abraded (sand paper) areas on the superior surface of the liver and the inferior surface of the diaphragm. This powder has been used effectively by Thompson to increase the blood supply to the heart in the treatment of myocardial ischemia. Its primary purpose would be the formation of an artificial vascular "bridge" between the portal and systemic veins to increase the vascular bed of the outflow tract of the liver. This method of treatment is appealing because of its simplicity. This is important when one considers that these patients are in the terminal phase of their disease and are extremely poor surgical risks. Further experience and a careful analy-

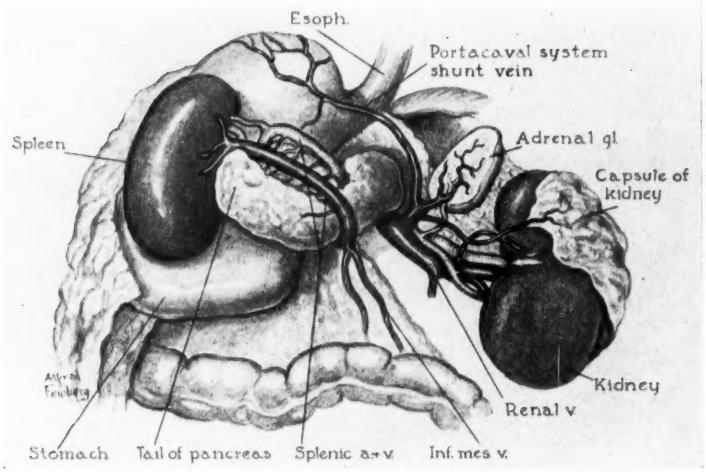

Fig. 14. Drawing to show a pre-existing portacaval shunt between the fundus of the stomach and the left adrenal vein. To demonstrate this, the stomach, spleen, and pancreas have been retracted to the right toward the midline. The left adrenal gland has been sectioned in the saggital plane.

sis of the results obtained will be necessary to permit a proper evaluation of the operation. The use of omentum as suggested by Drummond and Morison and Talma is objected to because the vascular communications that may form between the portal and systemic veins are through the inflow rather than the outflow tract of the liver. The effectiveness of resection of the lower portion of the esophagus and a part or all of the stomach is questionable when one considers the fact that the varices may have extended into the jejunum (Fig. 11).

An observation of particular interest is the apparent high incidence of previously existing or natural occurring portacaval shunts. In a study of 8 unselected fresh cadaver specimens, in all of which the livers were normal, a shunt was present in 4 (50 per cent). In each specimen the portal system was injected through one of the sigmoid veins, using a blue colored solution of liquid latex. The presence of a shunt was detected by the immediate filling of the inferior vena cava and the renal veins with the injected latex dye. Upon dissection of the 4 specimens in which shunts were present, in 2 the sites of communication were identified. In 1, the vein that formed the shunt was 4 millimeters in its narrowest diameter and extended from the fundus of the stomach to the left adrenal vein (Fig. 14). In the other, a vein, 3 millimeters in its narrowest diameter, formed a shunt between one of the veins in the mesentery of the terminal ileum and the right ovarian vein (Fig. 12).

There are many queries without conclusive answers relative to the use of portacaval shunts in the treatment of portal hypertension. Why do some patients with demonstrable and symptomatic esophageal varices have normal portal venous pressures if varices are considered due to portal hypertension? Why do some patients with portal hypertension have esophageal varices and no ascites? Why do some patients with cirrhosis of the liver and ascites, in all of whom there is a portal hypertension, have esophageal varices and others do not? What is the explanation for the spontaneous disappearance of esophageal varices? What is the explanation for the origin of esophageal varices in infants 6 to 12 weeks of age in many of whom at necropsy no evident cause is demonstrable? In addition to these there are many other questions which remain unanswered. Accordingly it is believed that from the observations of the study

presented our present concepts of portal hypertension, particularly in relation to its pathogenesis, classification, and treatment, should be re-examined.

CONCLUSIONS

It is postulated that the primary factor in the formation of ascites is an obstruction of the outflow tract of the liver, namely, the hepatic veins. In cirrhosis of the liver with irreversible ascites the obstruction is due to an obliterative fibrosis of the intrahepatic systemic venous bed. In cirrhosis of the liver with acute but reversible ascites, the obstruction is primarily due to intrahepatic cellular edema and congestive hepatomégaly secondary to both protein and electrolyte imbalances. In congestive heart failure and chronic constrictive pericarditis the obstruction of the outflow tract is due to intrahepatic cellular edema and congestive hepatomegaly secondary to chronic venous stasis in the thoracic segment of the inferior vena cava.

Pre-existing or natural occurring portacaval shunts are believed of frequent occurrence in the normal human. Such were present in 4 (50 per cent) of 8 unselected fresh cadaver specimens studied.

The treatment of cirrhosis of the liver with irreversible ascites by the performance of extrahepatic portacaval shunts, ligation of the hepatic artery, or by the establishment of an arteriovenous fistula between the hepatic artery and the portal vein are believed interdicted. The ideal in treatment is to increase the vascular bed of the outflow tract of the liver. A suggested method, used in 2 patients, is the formation of an artificial "bridge" between the portal and systemic veins by the application of magnesium trisilicate powder to abraded areas over the superior surface of the liver and the inferior surface of the diaphragm.

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PRIMARY AND SECONDARY OVARIAN ADENO-ACANTHOMA

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THE term "adeno-acanthoma" is employed to designate an adenocarcinoma in which few or many of the constituent elements exhibit malignant metaplasia to cells of a squamous type. This metaplastic transformation is perhaps not surprising when it is observed in connection with cancers arising from squamocolumnar junctional zones, such as exist in the endocervix and the lower reaches of the esophagus. On the other hand, considerably more interest is aroused when adeno-acanthomas are found affecting organs like the gallbladder which, even in embryonic life, are strictly of glandular composition. The observations of Sampson and of Kuzma and Moss and Runals that ovarian endometriosis may undergo malignant change cast an interesting sidelight on the problem, since in some of the cases, adeno-acanthoma, rather than adenocarcinoma, is the end product.

In a review of a large number of ovarian carcinomas, the author encountered no less than 40 examples of this interesting type of neoplasm. Data from these 40 cases, along with a review of the sparse literature on the subject, form the basis for the present report.

REVIEW OF THE LITERATURE

Although adeno-acanthoma was established as an entity almost 50 years ago by Herxheimer, it has only been in the past decade that primary adeno-acanthomas of the ovary have been described. The author had the privilege of casting a minority vote on the question of the nature of the tumor studied by Simpson and Branch, who finally favored a diagnosis of atypical Brenner tumor. The pertinent literature on 8 subsequent cases is well summarized in a recent article by Kistner and Hertig who, in reporting their own series, brought to 14 the current number of primary ovarian tumors of this type in the literature. There was some doubt whether the lesion in 1 of Kuzma's cases should not have been listed as an example of metastatic ovarian adeno-acanthoma inasmuch as a small (primary?) focus of adeno-acanthoma was found to involve the endometrium at hysterectomy. Kistner and Hertig found reports on 5 adeno-acanthomas originating in the endometrium and metastasizing to one or both ovaries. They recorded observations on 2 such cases in which they had been consulted. It would appear, therefore, that less than 25 cases exist in which adeno-acanthomas have involved the ovaries either as primary or as metastatic tumors.

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MATERIALS AND METHODS

The present study is a by-product of the author's researches on functioning ovarian tumors and of several Mayo Foundation theses on ovarian neoplasms carried out in the laboratory of surgical pathology. Some 2,000 solid and cystic ovarian neoplasms were available for study—all preserved in a 10 per cent solution of formalin. Original slides and new sections were made from freshly cut blocks of tissue. Forty tumors, or 2 per cent, exhibited a microscopic mixture of adenocarcinoma and squamous-cell carcinoma. Clinical histories in these cases were studied in detail and pertinent data were tabulated on suitable cards. The pathologic specimens were again assembled and scrutinized. Scale drawings were made and notes inserted on such features as the gross character of the ovarian lesions and the presence or absence of old hemorrhage or adhesions. A careful search was made for evidence of endometriosis. Particular attention was paid to the endometrium for evidence of malignant foci in those cases in which original reports were "negative."

Many blocks of tissue were cut routinely from the ovarian tumors, the tubes, and from

the posterior aspect of the uterus, and the endometrium when the latter material was available. These blocks were cut by the freezing and by the paraffin methods and stained routinely with hematoxylin and eosin. In 13 instances there was unquestioned evidence that the lesion arose in ovarian tissue. This group is hereinafter designated by the term "primary." In the remaining 27 cases, hereinafter referred to as the "secondary" group, inability to exclude the presence of endometrial involvement placed the ovarian tumor as being either a metastatic nodule or the result of independent primary neoplasia.

CLINICAL FEATURES

Age. The average age of patients with lesions in the primary group was 44.5 years, with extremes of 29 and 60 years. Five of the 13 patients were less than 40 years of age. Age data for patients with lesions in the secondary group were comparable, 5 of 27 patients being less than 40 years of age. When it is considered that 10 of the entire group of 40 patients were "young" women, it becomes apparent that this type of genital malignant process tends to affect persons at an earlier period of life than do ovarian and endometrial adenocarcinoma. Hertig has made a similar observation.

Marital status and parity. Thirty-five of the 40 patients were married and 21 of them had borne viable offspring. The incidence of sterile matings (14, or 40 per cent) was somewhat higher among those who had primary lesions than among those who had secondary lesions. The difference was not striking, but it does support the observation that ovaries which are the seats of primary carcinoma tend to be functionally defective. It might also strengthen the notion that ovarian endometriosis, a known etiologic factor in infertility, may have been operative in some of these cases. One patient was pregnant.

Symptoms. The list of general symptoms complained of by patients in both groups was as impressive as the lack of specificity of these symptoms for directing a diagnosis of pelvic malignancy. Four patients complained of no symptoms; 1, by contrast, listed "many doctors." Pain, usually pelvic, and either of a dull, dragging nature or coming on in attacks, had been noted by 4 patients with lesions in the primary and by 8 whose lesions were in the secondary groups. Abdominal bloating or the presence of a tumor had signaled the onset of trouble in 19 of the 40 patients with approximately the same incidence in both groups. Weakness, loss of weight, constipation, and urinary frequency were among the incidental symptoms.

As regards menstrual aberrations, 2 of 10 premenopausal women in the group with primary tumors complained of dysmenorrhea. In 1 of these, the dysmenorrhea had been so severe over a 12 year period that surgical treatment in the form of presacral neurectomy had been planned for relief of the condition. At operation, severe pelvic endometriosis, with a perforating primary right ovarian adeno-acanthoma was found. Other menstrual difficulties were infrequent among patients in this group. Involvement of the endometrium in patients with tumors in the secondary group gave rise to irregular bleeding and to postmenopausal spotting in almost all cases. Duration of these symptoms had been from 1 to 12 years.

Under a listing of "symptoms of endometriosis," inquiry was made concerning dyspareunia, co-menstrual pelvic tenderness, and so forth. Reasonably acceptable evidence pointing to the presence of this disorder was encountered in 4 patients only, 2 from each group. The signs elicited upon physical examination served to emphasize the adage that ovarian carcinoma is a silent menace. In 10 of the 13 patients with lesions in the primary group the principal finding was that of a pelvic mass. By no means was the location of this mass ascertained to be ovarian. Two patients exhibited tenderness on bimanual pelvic examination. No large ovaries were felt, but the presence of small, tender nodulations in the cul-de-sac led to a diagnosis of pelvic endometriosis. In 1 of these patients there was a tender nodule in the rectovaginal septum which had remained after subtotal hysterectomy (carried out elsewhere) for pelvic endometriosis. In the thirteenth patient a diagnosis of recurrent pelvic malignant process was arrived at more on the basis of tissue

Fig. 1. Primary bilateral solid ovarian adeno-acanthomas in a patient who had undergone subtotal hysterectomy previously for extensive endometriosis with an irremovable adenomyoma of the rectovaginal septum. Endometriosis remained in both ovaries and in the posterior portion of the cervix.

received from a former operation plus the finding of local fixation of the uterus.

Among patients with lesions in the secondary group the discovery of a pelvic mass was made in 21 instances. Enlargement of the uterus plus the presence of a bloody discharge emerging from the endocervical canal sometimes suggested the coexistence of endometrial malignancy. In 2 instances the patients came to the clinic because of uterine bleeding after removal (done elsewhere) of an ovarian adeno-acanthoma.

TREATMENT AND PROGNOSIS

Primary lesions. Treatment which it was hoped would cure these patients in general consisted of total hysterectomy, followed in most instances by postoperative therapy with roentgen rays. Total hysterectomy was accomplished as an original curative procedure in 9 of the 13 patients whose lesions were in the primary group. In 2 additional patients who underwent hysterectomy, the primary ovarian neoplasm had been removed elsewhere. In 1 of these, a metastatic or independent primary adeno-acanthoma was found in the remaining ovary. In 1 instance the ovarian carcinoma was bilateral, and so extensive that total hysterectomy did not completely eradicate all the neoplastic tissue. This operation, although radical, was considered palliative. In the thirteenth patient bilateral oophorectomy was performed at the clinic for a low grade encapsulated ovarian adeno-acanthoma in a 30 year old woman. No residual carcinoma was found when the uterus and tubes were removed 13 years later.

There were no operative deaths in the group of 13 patients with primary tumors. One patient was seen too recently for inclusion in a study of end results. Of the remaining 12 patients, 4 have succumbed from recurrent carcinoma at periods varying from 9 months[1] to 12½ years. One additional patient died from the effects of carcinoma of the stomach. Surgical pelvic exploration, carried out for this patient at the time of cholecystectomy performed several years after the ovarian tumor had been removed, had given negative results. The remaining 7 patients were all living and had been well for postoperative periods of 5 to 24 years at the time of this writing.

Secondary lesions. For the patients with secondary lesions treatment was somewhat similar to that described, but the operations were more frequently palliative since, with involvement of both uterus and ovaries, the tumors were sometimes of a more extensive nature. Seven of the patients were found to have obvious implants, and from 1 only biopsy material was removed. Bilateral ovarian involvement was present in 7 instances. Five patients of the group of 27 had undergone removal of one or both ovaries or the uterus prior to registration at the clinic. In several instances, a diagnosis of endometrial carcinoma had been made elsewhere, and radium had been used in treatment. Eventually, 22 patients underwent total hysterectomy with bilateral salpingo-oophorectomy, either at one operation or in several stages. In 1 patient who had symptoms suggesting endometrial carcinoma, curettage demonstrated benign endometrium. A bloody discharge persisted, and 6 months later an ovarian tumor was diagnosed and removed,

[1]Two patients with bilateral grade 3 neoplasms succumbed within the first postoperative year.

with the other ovary and the uterus. The latter was the seat of a duplication; in the horn was a carcinoma which the surgeon had failed to find in his previous curettement.

Of the 27 patients who had secondary ovarian adeno-acanthoma, 1 died immediately postoperatively, 5 were seen too recently to be included, and 3 patients have been lost to follow-up efforts. Hence, 18 of the 27 patients finally constituted the group among which 5 year survival studies could be made. Of these, 9 are dead, having succumbed in periods of from 2 months to 12 years postoperatively. In 1 of these patients with a diffuse grade 1 adenocarcinoma of the endometrium and with bilateral ovarian tumors, each 8 centimeters in diameter, recurrence developed 7 years postoperatively, yet the patient survived for 5 additional years. Nine or 50 per cent of the 18 patients among whom follow-up studies were made survived past the 5 year mark and at the time of this report were free from carcinoma, so far as could be determined.

GROSS AND MICROSCOPIC PATHOLOGIC FEATURES

Primary lesions. In this group of 13 patients there were 18 primary tumors, with bilateral ovarian involvement in 5 of 13 cases. In 4 of these the gross appearance suggested multiple primary sites of origin, and in the fifth case involvement of one ovary appeared to represent implantation metastasis. In the remaining 8 cases there was gross evidence of carcinoma in one ovary only.

The average size of the lesions was 11 centimeters, with ranges from 1 to 20 centimeters. Three were solid, 2 were cystic, and the remainder could best be described as "cystadenocarcinomas exhibiting solid areas of carcinoma, usually on their internal surfaces." Ten lesions showed fair degrees of encapsulation; the remainder were found to be either ruptured or adherent to surrounding tissues. In 4 of the cystic tumors a distinctly tarry content suggested possible association with endometriosis. In 2 cases there was widespread peritoneal carcinomatosis. None of the 11 uteri available for study showed evidence of endometrial carcinoma. Four contained leiomyomas, 8 endometriosis (5 also with endometriosis involving the sound ovary) and in 1 patient there was a large adenomyoma of the rectovaginal septum (Fig. 1). One uterus had been the seat of a pregnancy (Fig. 2); two exhibited carcinomatous implants on the serosal surfaces. Concerning 2 uteri which were not removed, benign endometrial curettings were available and since the patients in question lived 13 and 11½ years, respectively, postoperatively, their ovarian tumors were placed in the primary group.

Fig. 2. Decidual reaction in an area of pelvic endometriosis in a patient whose pregnancy was complicated by recurrent ovarian adeno-acanthoma. Hematoxylin and eosin, ×159.

Microscopically, 1 of the neoplasms appeared to represent malignant squamous metaplasia in a mixed serous and mucinous cystadenocarcinoma. In 2 instances the degree of cellular dedifferentiation was such as to preclude accurate appraisal of the cell of origin. The remaining tumors could best be described as being much more typical of endometrial than of ovarian cancer (Fig. 3), and in 2 an origin from endometriosis could be traced definitely (Figs. 4 and 5). In 9 of the 13 cases the tumors exhibited areas in which benign epithelium was present which was neither ciliated nor mucus-producing (Fig. 6). In 4 instances this benign epithelium was associated with an endometrial-like stroma. In 2 of these 4 tumors there were transition zones between benign and malignant areas, hence the lesions are considered by the author to represent malignant neoplasia originating in endometriosis.

Since all the 18 tumors contained both glandular and squamous elements, grading them was a matter of little difficulty. With the use of Broders' method, 8 of the tumors were grade 1, 6 were grade 2, and 4 were grade 3 adeno-acanthomas.

Fig. 3. Well differentiated adenocarcinoma with malignant metaplasia to cells of a squamous type. The dense stromal reaction seen in this adeno-acanthoma was repeatedly observed in both primary and secondary lesions. Hematoxylin and eosin, ×74.

Secondary lesions. In this group of 27 patients there were 34 tumors. In general, the ovarian characteristics of the secondary tumors did not differ sufficiently from those of the primary tumors to merit a separate detailed description. Bilaterality was a feature in 7 cases, but only once was it obvious grossly that 1 of the tumors represented an implant. Among the 20 unilateral examples 3 had shaggy external surfaces, the remainder being rather smooth and more reminiscent of primary ovarian new growths.[1] Five of the tumors were solid, 6 were cystic, and the remainder exhibited a mixture of both of these characteristics. Adhesions were noted in a number of instances, particularly among patients in whom previous pelvic operations had been performed. Seven of the tumors were associated with tarry material. Eight of the 27 patients had peritoneal implants, including 3 who had advanced abdominal carcinomatosis.

[1]The difficulty of establishing by gross as well as by microscopic means whether a given ovarian tumor is primary or metastatic is well known.

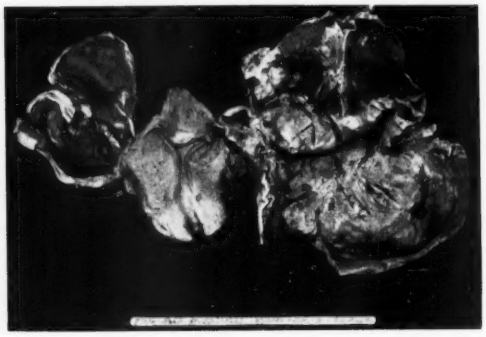
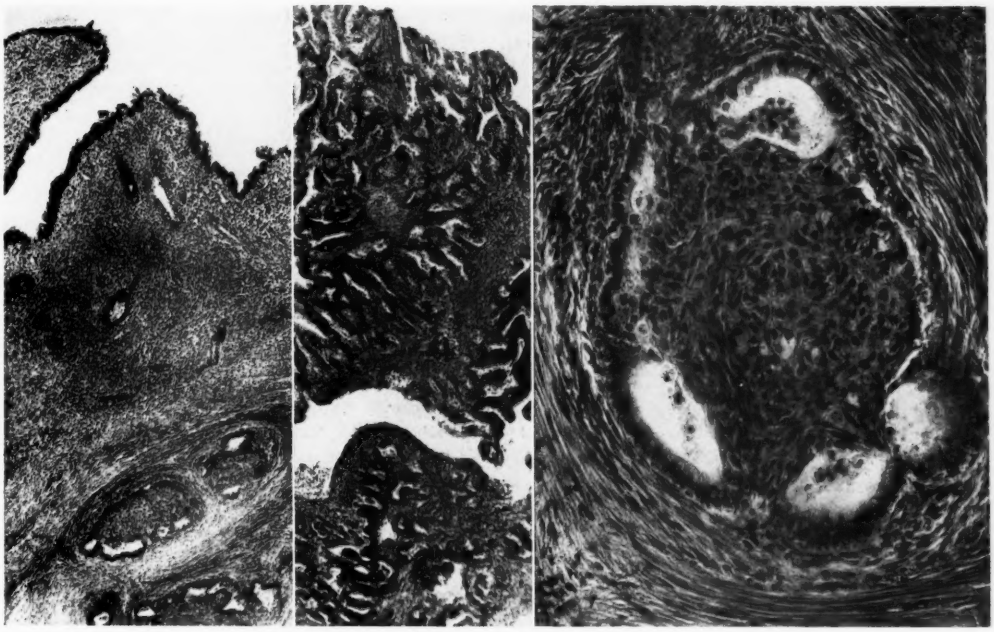


Fig. 4. Bilateral primary ovarian adeno-acanthomas occurring as solid nodules in the walls of cystic endometriomas filled with tarry material. Figures 5 and 7 are also from the same case.

The condition of the uteri warrants more descriptive detail. Twenty-two gross specimens of lesions from 27 women were preserved and available for examination. In 18 instances the amount of cancerous tissue involving the ovary or ovaries exceeded in bulk that present within the uterus (Fig. 7). In 11 of these cases the uterine lesion varied from 3 millimeters to 2 centimeters in diameter, suggesting the possibility of implantation from an ovarian primary lesion or the development of an independent carcinomatous focus in the endometrium. In 2 instances (1 apparently an endocervical carcinoma) the uterine growth, although circumscribed, was relatively large and could well have been the source for spread to the ovaries (Fig. 8). In 9 instances the endometrial carcinoma was diffuse, with penetration of the underlying myometrium for distances varying from 1 millimeter to the entire thickness of the latter. In 1 specimen such a diffuse carcinoma involved one horn of a double uterus.

In 5 cases uteri were not available for study. Regarding 2 patients of these 5, the surgeon reported uterine involvement in malignant masses that were irremovable. Three others had undergone salpingo-oophorectomy elsewhere and had refused further operations at this institution. One of these 3 patients subsequently died, and necropsy was not done; another patient was seen too recently for evaluation of the endometrial status, while endometrial carcinoma subsequently was found in the third. Thus, the lesions of 4 of this group of 5 patients possibly belong in the primary category. However, by the terms of our definition we elected to consider the ovarian tumors of these 5 patients as secondary. It is of interest to note that for only 5 of the 27 patients who had



a b c

Fig. 5. a, Typical glands and stroma of endometriosis are depicted in the upper portions and nests of adeno-acanthoma in the lower portions of this photomicrograph. Hematoxylin and eosin, ×33. b, From a predominantly adenocarcinomatous area of 1 of the tumors. Hematoxylin and eosin, ×33. c, High power view of an area showing the typical picture of adeno-acanthoma with central squamatization and a peripheral clustering of malignant glandular acini. Hematoxylin and eosin, ×189.

secondary lesions was the diagnosis of endometrial carcinoma made prior to the discovery and removal of their involved adnexa.

As with the gross, the microscopic features of what we have chosen to call "secondary ovarian adeno-acanthoma" exhibited remarkably little difference from the microscopic features of the primary ovarian adeno-acanthoma. All the lesions contained glandular structures as well as pearly bodies. Pelvic endometriosis was present in 7 of the 22 cases, with tissue which was adequate for study in this regard. Thirteen of 34 ovarian specimens contained benign areas, and 4 had cells which were definitely ciliated. Psammoma bodies were observed in 3 tumors. Seventeen of the neoplasms were grade 1, 12 were grade 2, and 5 were grade 3 (Broders' classification). The grades of the uterine counterparts corresponded in all instances in which the endometrium was available for comparison. In none of the cases, however, could a direct connection be traced between the endometrial and the ovarian growths.

Among the cases of unilateral involvement, significant findings in the contralateral gonad consisted of endometriosis in 3, cystadenoma in 1, and dermoid cyst in 1 case, respectively. Study of the fallopian tubes did not prove or disprove their role as passive conduits for the spread of carcinoma from the endometrium to the ovary, or vice versa. Benign lesions present in 22 available uteri included endometriomas in 5 cases, fibromyomas in 6, adenomyomas in 2, and endometrial polyps in 3. As mentioned previously, the average size of removed uteri was somewhat larger than normal.

COMMENT

Incidence. The actual incidence of ovarian adeno-acanthoma is impossible to ascertain

from the literature. The lesions in the present series of 40 cases were discovered in a group of some 2,000 ovarian tumors, an incidence of 2 per cent. Since the majority of these 40 lesions were found among the last 500 tumors which were examined more diligently for evidences of the microscopic changes herein described, the author is certain that further sections cut and studied from the large volume of this material would bring to light additional examples.

Histogenesis. From the standpoint of histogenesis, processes from 4 tissues possibly account for the origin of primary and secondary ovarian adeno-acanthomas; namely, serous and mucinous cystadenocarcinomas, ovarian endometriosis, and metastases from an endometrial or an endocervical adeno-acanthoma.

The present series, like that reported by Kistner and Hertig, furnished evidence favoring each of these hypotheses. Several of the tumors contained psammoma bodies, a number exhibited areas of benign epithelium, many were associated with pelvic endometriosis, and in at least 2 instances there was evidence that the ovarian tumor had arisen by means of malignant metaplasia in such tissue.

It has been observed by the author that carcinomas originating in endometrial tissues of young women are associated with a high incidence of adeno-acanthoma. Indirect clinical evidence presented in this series relates the age of the patient, at least, to such a concept of histogenesis. Without a doubt, certain of the ovarian lesions in the group designated as secondary were truly metastatic. However, the fact that many of the endometrial foci were small and resembled implants, coupled with the amazingly good outlook for patients with combined endometrial and ovarian lesions, strengthens the notion that this strange combination frequently represented the development of separate primary growths. The high incidence of pelvic endometriosis among patients with endometrial and ovarian tumors supports, rather than depreciates, this last mentioned theory of histogenesis. In neither location was it evident just what stimulus had given rise to the malignant metaplasia from glandular to squamous cells. To trace the change to muellerian cell potentials seems absurd when it is observed that nonmuellerian appendages like the gallbladder exhibit a similar incidence of adeno-acanthoma within malignant neoplasms arising in that organ.

Clinical features. As noted by Hertig, the salient clinical features common to these two groups of patients were an average age considerably less than that reported for patients with ovarian cancers in general, and a somewhat reduced incidence of fertility. The association of endometrial carcinoma gave a high incidence of abdominal bleeding among patients with lesions in the secondary group, but in most other respects no salient differences were observed. It is impossible to diagnose ovarian adeno-acanthoma on a clinical basis alone.

Pathologic features. Pathologically, there was little in the gross examination of these tumor types to set them aside from each other or from an unselected group of ovarian carcinomas. The presence of hemorrhagic or tarry material in cystic examples and the coexistence of extensive pelvic endometriosis in certain cases might well be mistaken by the average surgeon for degeneration and necrosis, on the one hand, and malignant infiltration, on the other. There was a decreased tendency toward generalized abdominal carcinomatosis, however, and on gross inspection the existence of "jelly belly" was not observed as accompanying either primary or secondary tumors. Likewise, none of the lesions had the typical cauliflower appearance of well advanced serous cystadenocarcinoma. Gross evidences of calcification were lacking even when, as in 2 cases, the omentum was massively infiltrated by tumor tissue.

Microscopically, although papillary formations and psammoma bodies were noted occasionally, the ovarian lesions as well as their uterine counterparts histologically were very reminiscent of endometrial carcinoma. Like Hertig, I have been so impressed by this histologic mimicry that I have employed the term "endometrial-like carcinoma" for one major group of ovarian tumors. The existence in all cases of areas exhibiting malignant metaplasia to squamous cells heightens this resemblance. The high incidence of associated

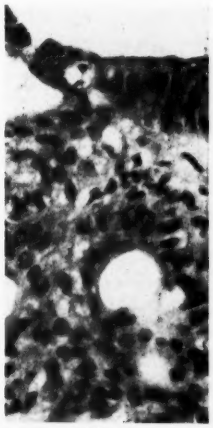
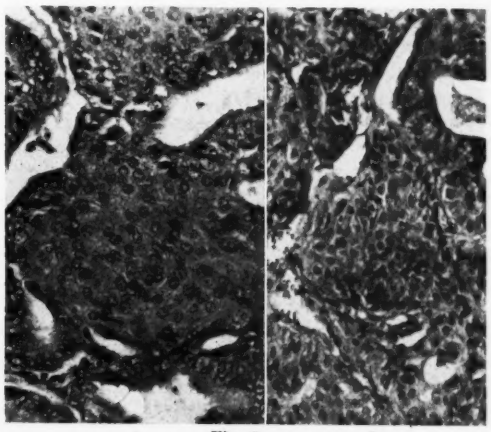


Fig. 6.



a Fig. 8. b

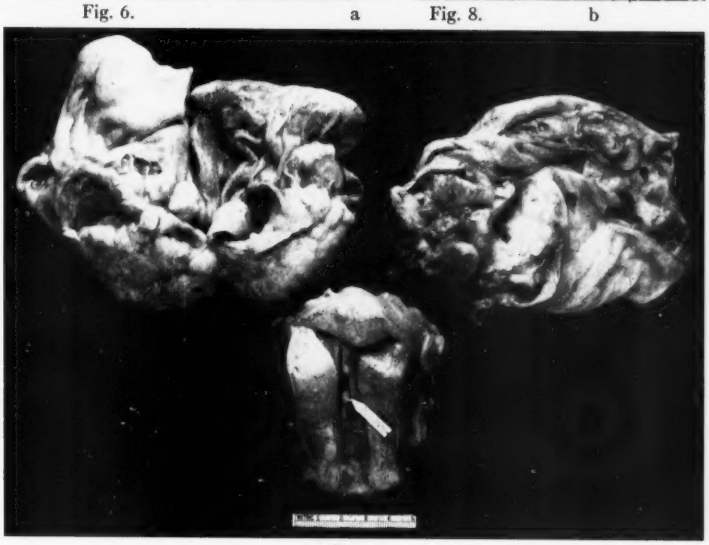


Fig. 7.

Fig. 6. The finding of benign areas in the lesion depicted in Figure 8 is strong evidence that this ovarian tumor was not metastatic. Hematoxylin and eosin, ×327.

Fig. 7. Bilateral secondary (so-called) ovarian adeno-acanthoma with a very small uterine counterpart. It is difficult to accept the current notion that ovarian tumors, under these circumstances, are metastatic.

Fig. 8. a, Section from a large endometrial adeno-acanthoma. Hematoxylin and eosin, ×185. b, Grade 2 ovarian adeno-acanthoma from the patient whose uterine tumor is shown in Figure 8 a. Hematoxylin and eosin, ×172.

pelvic endometriosis and the frequent finding of benign areas within both the primary and secondary tumors in this series increase the likelihood that many of the ovarian tumors actually did originate in ectopic endometrium. As mentioned previously, 2 tumors in the primary group could be so traced, to the author's satisfaction.

Treatment. The treatment of ovarian adeno-acanthomas, whether unilateral or bilateral, should be double salpingo-oophorectomy with hysterectomy and postoperative therapy with

roentgen rays. Those who would conserve an "innocent" uterus or a "sound" ovary in the presence of unilateral adnexal tumors should consider the ample evidence that recurrence is the price paid for conservatism. It is to be recalled that in this series, malignancy was confined to the ovaries in only 13 of the group of 40 patients, and that uterine carcinoma was discovered in a number of patients who previously underwent less than radical surgical management. In our series of patients the best results were obtained when it was possible to carry out the ideals of management which have been outlined.

Prognosis. Considered as an individual group, the 50 odd per cent of patients with primary and secondary ovarian adeno-acanthomas who survived for 5 years is surprisingly good. It compares very favorably, in the matter of end results, with survival rates associated with all other ovarian carcinomas, except possibly mucinous cystadenocarcinomas and low grade papillary serous lesions. What is even more arresting is the fact that a relatively large number of our patients with lesions designated as secondary, successfully passed the 5 year mark postoperatively. It is known that 5 per cent of ovarian cancers metastasize to the endometrium, and that the latter "returns the malignant compliment" to the extent of about 2.5 per cent. In either case such spread between these two areas implies a very bad prognosis. The relatively good outlook for patients who have both ovarian and endometrial involvement points, I believe, to multicentric foci of origin rather than to a process of metastasis.

SUMMARY AND CONCLUSIONS

Data are presented concerning a group of 40 patients whose ovarian tumors exhibited the unusual picture of adeno-acanthoma. The incidence of the lesion was 2 per cent. In 13 cases in which the lesions were designated as primary, the presence of endometrial carcinoma was excluded. In 27 patients ovarian involvement could possibly have been metastatic from a primary endometrial neoplasm. Although the lesions of these 27 patients were designated as secondary for the purposes of this paper, the endometrial growths could well have represented independent foci of neoplasia. In a fair proportion of secondary cases evidence favored an interpretation based on metastasis from ovary to endometrium. Both primary and secondary ovarian adeno-acanthomas appeared to affect women in young age brackets and were associated with an increased incidence of infertility.

Pathologically, the tumors resembled endometrial, rather than ovarian, cancer, and in both groups of patients they were very frequently associated with pelvic endometriosis. In 2 instances ovarian adeno-acanthomas could be traced in point of origin to such foci. Prognosis was good for patients in both groups, and was surprisingly so in respect to secondary ovarian adeno-acanthomas, which by definition comprised lesions with endometrial as well as ovarian involvement.

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THE RELATION OF PREGNANCY TO ABNORMALITIES OF THE CERVICAL EPITHELIUM

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RECENTLY we have reviewed the evidence supporting the widely accepted belief that pregnancy causes specific epithelial changes which may be confused with preinvasive carcinoma (9). We have also presented evidence which suggests that such a belief is erroneous (4, 9). These communications dealt solely with lesions considered to be preinvasive carcinoma. We have encountered epithelial abnormalities which are not preinvasive carcinoma. Data will be presented to show that these lesser abnormalities, found during pregnancy, also are not evanescent pregnancy changes.

As in past reports, these data have been obtained as a part of a larger study concerned with the cervix during pregnancy and the postpartum period. A few of these lesions were discovered as a result of random biopsies. Most, however, were found in biopsies of gross cervical abnormalities or more commonly because of a previous atypical or positive cytology smear. Fifteen of these 19 patients were from the Chicago Maternity Center. One each was from the Prenatal Clinic of Cook County Hospital, the outpatient clinic of Northwestern University Medical School, the obstetric clinic of Wesley Memorial Hospital, and from private practice. All but 2 were negroes.

Lesions variously termed equivocal, precancerous metaplasia, anaplasia, atypical basal cell hyperplasia, atypical hyperplasia of the stratified squamous epithelium, and dysplasia are definite entities to many investigators; on the other hand, they all lack abnormalities of sufficient degree to justify the diagnosis of preinvasive carcinoma. We do not include among these lesions simple or physiologic basal cell hyperplasia of the squamous epithelium. This consists of an increase in thickness of the basal cell layer (2 to 4 cell layers instead of the usual single layer of cells), but with no abnormal or atypical nuclei being present. We believe this to be a physiologic basal cell hyperplasia due merely to rapid growth of the ectocervical epithelium and we also recognize that the frequency of this change, as well as the frequency of hyperplasia and metaplasia (termed reserve cell hyperplasia by Hellman and associates) of the glandular elements of the cervix, is increased in pregnancy.

We have divided the true abnormalities into equivocal lesions and atypical basal cell hyperplasias. The latter diagnosis is made by us when abnormalities do not extend throughout the full thickness of the epithelium, and the cells and nuclei of the superficial layers seem normal. The diagnosis of equivocal lesion has been reserved for those specimens in which nuclear atypia, though extending through the full thickness of the epithelium, is less marked in the superficial layers than is observed in well differentiated preinvasive carcinoma. This diagnosis is also applied to lesions in which the findings are similar throughout the full thickness but the nuclear atypia and disturbances in nuclear/cytoplasmic ratio, nucleolar/nuclear ratio, and the number of mitotic figures are believed by us to be insufficient to justify the diagnosis of preinvasive carcinoma. The likelihood that a lesion will be termed equivocal rather than carcinoma increases with an increasing degree of differentiation or maturing of cells and a lessening of pleomorphism or abnormal variations in size and shape of the nuclei. It is therefore inevitable that borderline lesions are found where classification is difficult. We

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TABLE I.—ATYPICAL BASAL CELL HYPERPLASIA IN PREGNANCY

A. Disappeared

Patient No. Name	Date[1]	Age, years[2] Grav. Para.	Antepartum			Postpartum			Comments
			Weeks	Smear	Biopsy	Weeks	Smear	Biopsy	
1. O.C.	June 1953	27 G 5 P 5	30	Neg.	(4) BCH	16	Neg.	(4) Neg.	

B. Persisted or progressed

2. L.A.	March 1952	18 G 2 P 2	29–31	Neg.	(2)*BCH	6 12		(1) BCH (4) BCH	This patient No. 17, of previous report (3). *Condyloma acuminatum
3. A.G.	Feb. 1949	19 G 4 P 4	25 31	Neg. Neg.	(1) BCH (1) BCH	8 15		(3) BCH (2) BCH	
4. M.S.	July 1950	33 G 10 P 8	22 25		(1) BCH (1) Neg.	13 14 17	Atyp	(1) Ca (4) Ca Equiv.(hyst)	
5. I.M.	May 1949	20 G 4 P 4	28 29	Atyp	(1) BCH	28		(4) Equiv	

Atyp—atypical; Pos—positive; Neg—negative; Uns—unsatisfactory; BCH—atypical basal cell hyperplasia; Del—delivery; Hyst—hysterectomy; Ca—preinvasive carcinoma; Equiv—equivocal lesion. The numbers in parentheses refer to the number of quadrants biopsied.

[1]Month and year of first smear or biopsy.

[2]Age at first smear or biopsy; gravity and parity after last pregnancy.

have tried to err on the conservative side in arriving at our diagnoses and, as one would expect, there is occasional disagreement among our own group (see Fig. 8a). Undoubtedly, there are individuals who consider some of the well differentiated preinvasive carcinomas in our previous reports as equivocal. However, *our major point, then as now, is that these lesions (whatever one may choose to call them) are not pregnancy changes* since *most of them have persisted well beyond the termination of pregnancy.*

This point apparently cannot be emphasized enough as quite recently our good friend Dr. Lou Hellman and others missed it after viewing, both in New York and Cincinnati, an exhibit based on some of this material and the previously reported preinvasive carcinomas discovered in pregnancy (4, 9). These authors cited the 3 cases of preinvasive carcinoma which could not be found postpartum, the implication being that this was the usual fate of such lesions. Apparently, they not only missed the point of the exhibit but also the fact that there were 16 other lesions presented all of which persisted postpartum.

Because of the large number of cases, it is not practical to publish photographs of all of them, as we would have preferred to do. In so far as is possible we have depicted representative specimens. Some of these lesions show considerable variation in different areas. The area considered most abnormal was, of course, the one selected for photography where technically possible.

The detailed data concerning each patient are presented in Tables I, II, and III. In each instance the number of quadrants biopsied is noted in parentheses. These biopsies were prepared as previously described (9) so that 8 levels in each of the 4 quadrants were sampled. Additional sections were made if necessary. Surgical cone and hysterectomy specimens were serially blocked and multiple sections cut from each block as necessary. The recorded age of the patient in the tables is that at the time of the first biopsy, whereas the parity is that at the last biopsy.

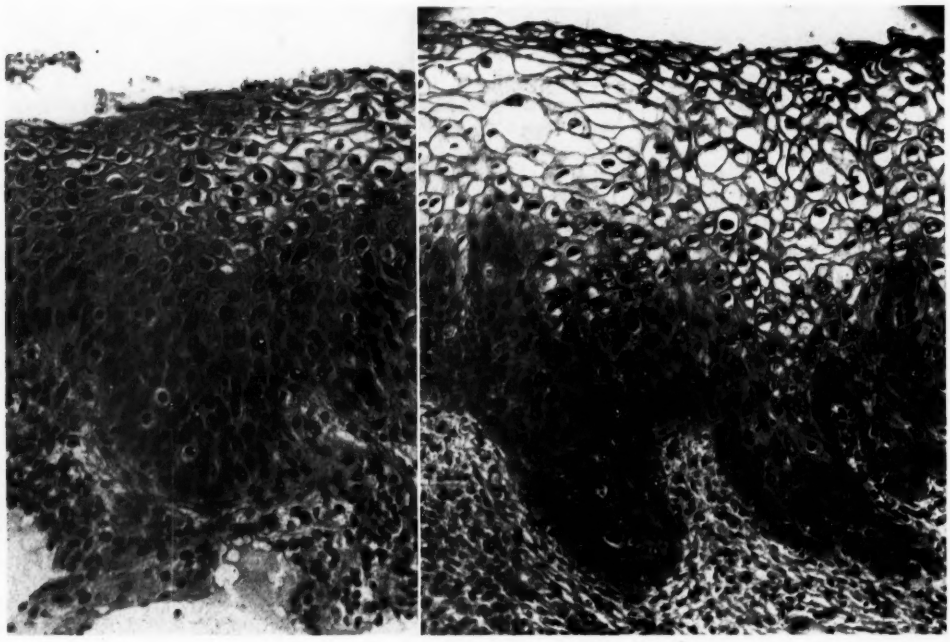
It is hoped that those who have read thus far will bear in mind that: (1) The subject of this paper is whether these abnormalities of the stratified squamous epithelium of the cervix are, or are not, evanescent pregnancy changes. (2) The fact that certain of these lesions have disappeared after the termination of pregnancy does not prove that they were self limited pregnancy changes, unless this disappearance rate is significantly greater than that of similar lesions found in nonpregnant patients.

TABLE II.—EQUIVOCAL LESIONS IN PREGNANCY

A. Disappeared

Patient No. Name	Date	Age, years Grav. Para.	Antepartum			Postpartum			Comments
			Weeks	Smear	Biopsy	Weeks	Smear	Biopsy	
6. P.H.	Jan. 1950	25 G 5 P 3	31 33		(1) Equiv (3) Equiv	17 49		(1) Neg (4) Neg	Lost
7. M.Jo.	Feb. 1951	23 G 2 P 2	10 11 28	Atyp Atyp Atyp	(4) Equiv	At del 8 mo		(4) Neg (4) Neg	
8. M.L.	June 1951	20 G 2 P 2	29 30 39	Pos Atyp Neg	(4) Equiv	1 11		(4) Equiv Neg (cone)	
9. A.P.	Dec. 1949	19 G 3 P 2	21 23 24 25	 Neg	(1) Equiv (1) Neg (2) Neg	8	Atyp	(2) Neg	
10. K.Y.	Sept. 1952	19 G 1 P 1	27 30 31 33	Atyp Atyp Atyp	 (1) Equiv (1) BCH	8		(4) Neg	This patient, No. 22, of previous report (3). Condyloma acuminatum in first biopsy.
B. Regressed									
11. M.Ja.	March 1952	28 G 5 P 5	14 17 36	Atyp Pos Atyp	(1) Equiv	11	Atyp	(4) BCH	Lost
12. A.M.	July 1953	20 G 4 P 4	31	Neg	(4) Equiv	14	Atyp	(4) BCH	
C. Persisted									
13. E.C.	May 1949	20 G 2 P 2	27 31		(1) Equiv (1) Equiv	7 23 37 41	Atyp Atyp	(1) Neg (1) Equiv Neg (hyst)	
14. S.C.	Jan. 1952	22 G 4 P 3	5 8	 Pos	(1) Equiv (4) Equiv	2 12 22	Atyp Neg Neg	(3) Neg (4) Equiv	Cervical cautery to stop bleeding after biopsy 2 weeks postpartum. Patient again pregnant
15. O.H.	Dec. 1949	34 G 4 P 4	35 37		(1) Equiv (1) Equiv	7 16 36 1 yr. 3 yr. and 10 mos.		(2) Ca (4) Equiv (1) Neg (3) Neg (4) Neg	
16. M.O.	Nov. 1949	20 G 3 P 2	27 29	Atyp Atyp	(1)* (3)*Equiv	16		(2) Equiv	This patient, No. 16, of previous report (3). *Condyloma acuminatum
17. R.C.	Jan. 1950	16 G 3 P 3	31 33 35		(1) Equiv (3) Neg (1) Equiv				This patient delivered first observed pregnancy elsewhere. There was 1 intervening pregnancy.
						12		(4) Equiv	
18. J.L.N.	Oct. 1951	23 G 4 P 4	33 34	Atyp	(1) Equiv (4) Equiv	6 17	Neg Pos	 (4) Equiv	Follow-up continues
19. E.B.W.	March 1951	17 G 2 P 2	7 13 24	Atyp Atyp	 (4) Equiv	25–27 28–31		(4) Equiv Equiv(hyst)	

We are unable to decide exactly how long pregnancy changes should be expected to persist. This should not be surprising since we do not believe that pregnancy per se causes any changes in the epithelia of the cervix characteristic of and limited to pregnancy. We do think the implication by Mullen and Foraker that such changes persist for ±6 months is unreasonable. Incidentally, it seems unfortunate that almost all of the publications having to do with pregnancy changes report histologic studies and tabulations on the cervical



a b

Fig. 1. Patient 2. a, NUMS16262. Antepartum biopsy, 29 to 31 weeks pregnant. Diagnosis: atypical basal cell hyperplasia. Nuclear crowding, disturbances of polarity, and hyperchromatism involving at least the lower half of the epithelium. ×209. b, NUMS16979. Postpartum biopsy at 12 weeks. Atypical basal cell hyperplasia similar to that in the antepartum biopsy. Again numerous mitotic figures (some abnormal) are present. This lesion was not found during the next pregnancy, but postpartum an identical abnormality was present. ×185.

epithelia of pregnant women, but fail to compare such data with the findings in a comparable group of nonpregnant women (for exceptions see references 1, 5). The fact that a certain finding is present in x per cent of pregnant women does not prove that it is a pregnancy change unless comparable data are available to show that this certain finding does not occur with similar frequency in nonpregnant women.

Many of the patients presented here have been followed for a considerable period of time (up to 4 years and 11 months) and in 7 of the patients through 2 or more pregnancies (maximum of 4). To avoid too large a mass of confusing details we will not present the lengthy follow-up material which we have collected in each case but only (with a few exceptions) the findings noted during and after the first observed pregnancy.

TABLE III.—BASAL CELL HYPERPLASIA TO PREINVASIVE CARCINOMA

Patient No. Name	Date	Age, years Grav. Para.	Antepartum			Postpartum			Comments
			Weeks	Smear	Biopsy	Weeks	Smear	Biopsy	
20. L.R.	May 1950	22 G 5 P 4				7 14	Atyp	(1) BCH	First biopsy taken about 1 wk. prior to conception
			5–6 22	Neg Neg	(4) BCH (4) Equiv	11		(2) Neg	
			5 38	Neg	(4) Ca	13 17	Neg	(4) Ca	

ATYPICAL BASAL CELL HYPERPLASIA

The original biopsies from 5 pregnant patients showed atypical basal cell hyperplasia. Four of these 5 lesions persisted (or progressed). In 1 patient (No. 1) the lesion found at the thirtieth week of pregnancy could not be found 16 weeks postpartum.

Patient 2[1] was biopsied because of a grossly papillomatous lesion of the cervix. Adjacent to this lesion there was an atypical basal cell hyperplasia. Postpartum no papilloma was present but biopsy on 2 occasions (6 and 12 weeks) revealed the atypical basal cell hyperplasia (Fig. 1). In Patient 3 the basal cell hyperplasia discovered in the twenty-fifth week of pregnancy was present in biopsies at the eighth and fifteenth week postpartum. Patient 4 had a basal cell hyperplasia in 1 of 2 quadrants biopsied during pregnancy (Fig. 2a). Postpartum a preinvasive carcinoma was present in biopsies made in the thirteenth and fourteenth weeks (Fig. 2b). In the hysterectomy specimen at 17 weeks postpartum, serial blocks from the cervix revealed only an equivocal lesion. Patient 5 had an atypical basal cell hyperplasia in 1 quadrant in the twenty-eighth week of pregnancy (Fig. 3a). Twenty-eight weeks postpartum an equivocal lesion (Fig. 3b) was noted (apparent progression from the previously discovered basal cell hyperplasia). At this point the patient refused further care. She was not seen again for almost 4 years. During this time she had been delivered elsewhere of 2 term pregnancies. When seen and biopsied 15 months after her last delivery, which was 3 years and 11 months after the equivocal lesion had been found, the biopsies were negative. The lesion apparently had disappeared in the interim. Please note, however, that the original abnormality discovered during pregnancy did not disappear during the puerperium but was found to have progressed to an equivocal status at 28 weeks postpartum—an unlikely pregnancy change.

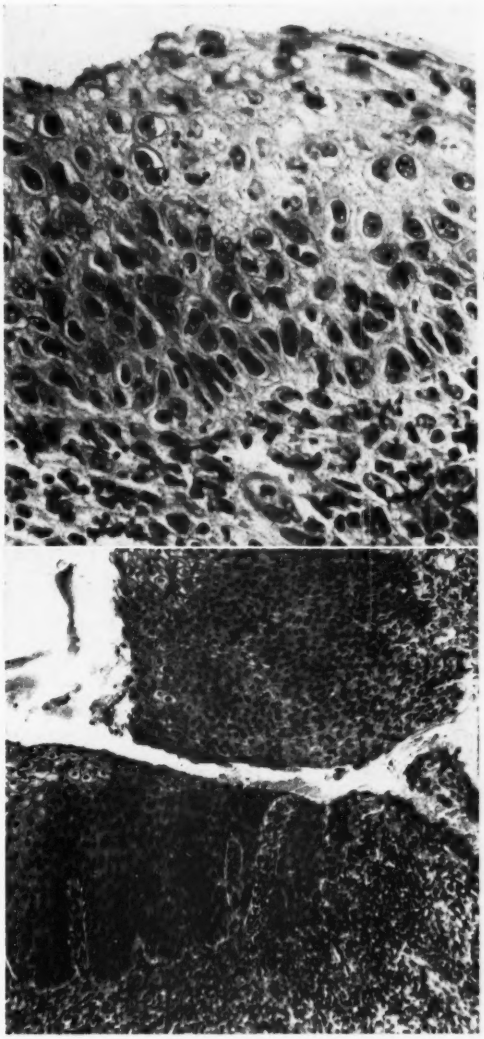
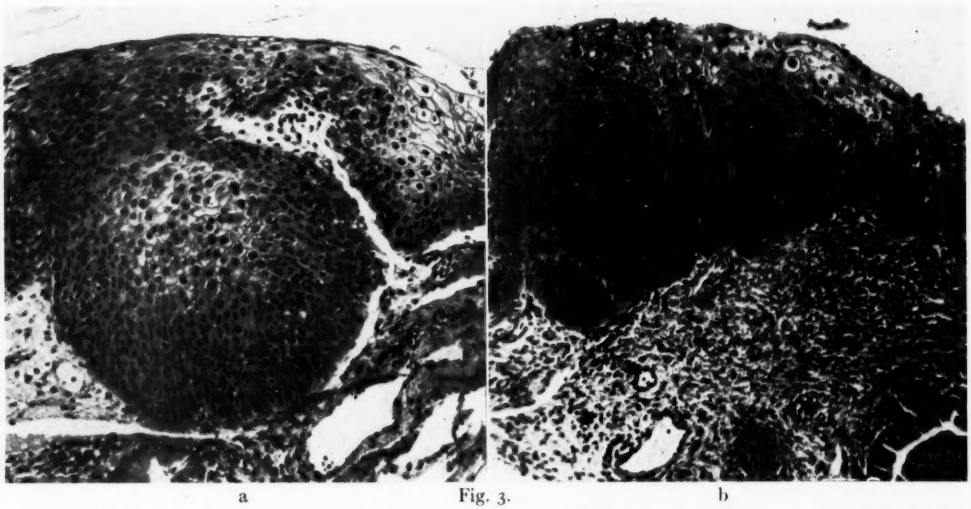


Fig. 2. Patient 4. a, NUMS13202. Antepartum biopsy at twenty-second week of pregnancy. Moderate nuclear atypia with disturbed polarity in lower ½ to ⅔ of the epithelium. Diagnosis: atypical basal cell hyperplasia. ×378. b, NUMS14236. Biopsy at 13 weeks postpartum. Nuclear abnormalities extend through the full thickness of epithelium even though there is some maturing of the cells as they near the surface. Diagnosis: well differentiated preinvasive carcinoma. ×104.

EQUIVOCAL LESIONS

Fourteen patients had equivocal lesions during pregnancy and have been followed through one or more pregnancies. For purposes of discussion these patients have been divided into three groups, namely those in which the lesion either (1) disappeared, (2) regressed, or (3) persisted. The equivocal

[1]This patient was No. 17 of a previous report (3).



a Fig. 3. b

F 3. Patient 5. a, NUMS11439. Antepartum biopsy at 28 weeks. Nuclear abnormalities marked in the lower ⅓ to ½ of the epithelium; an atypical basal cell hyperplasia. ×117. b, NUMS12548. Postpartum biopsy at 28 weeks. Moderate nuclear abnormalities extending through the full thickness of the epithelium though superficial layers show considerable differentiation; an equivocal lesion. Biopsy 3 years and 11 months (and 2 pregnancies) later showed only cervicitis. ×117.

Fig. 4. Patient 8. NUMS14779. Biopsy at 1 week postpartum. Marked nuclear atypia throughout epithelium, an equivocal lesion. Antepartum biopsy was identical. No abnormality was found in the cone amputation done at 11 weeks postpartum (see text). ×340.

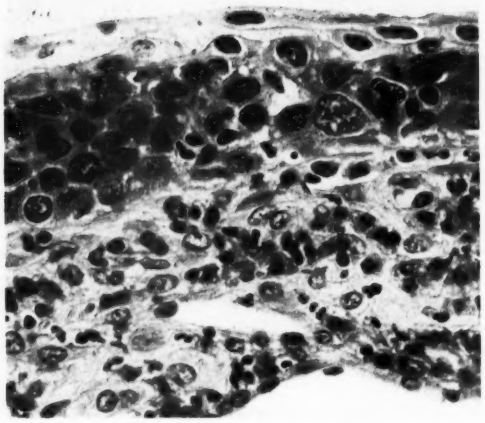


Fig. 4.

lesions which could not be found postpartum are listed in Table II,A. In Patient 8 an equivocal lesion was demonstrated in the thirtieth week of pregnancy. One week after delivery a 4 quadrant biopsy was performed, and an identical lesion was found (Fig. 4). Subsequent cone amputation at the eleventh week postpartum failed to demonstrate any abnormality of the squamous epithelium. This lesion, obviously, must be considered to have disappeared. In Patient 10[1] postpartum biopsy at 8 weeks was negative. Unfortunately, this patient has been lost. The other 3 patients have been followed for a considerable period of time postpartum with no demonstrable abnormality in any of the subsequent biopsies.

In Table II,B are listed the 2 patients in whom the equivocal lesion was not found postpartum. However, the squamous epithelium in these biopsies was not normal, since an atypical basal cell hyperplasia was present. The lesions in these patients are considered to have regressed. Follow-up, unfortunately, cannot be considered adequate in 1 of the 2 patients. Patient 11 (Fig. 5) has been lost after a relatively short post-

[1]Patients 10 and 16 were 22 and 16 respectively of a previous report. Pictures of the lesion in Patient 10 appear in that publication (3).

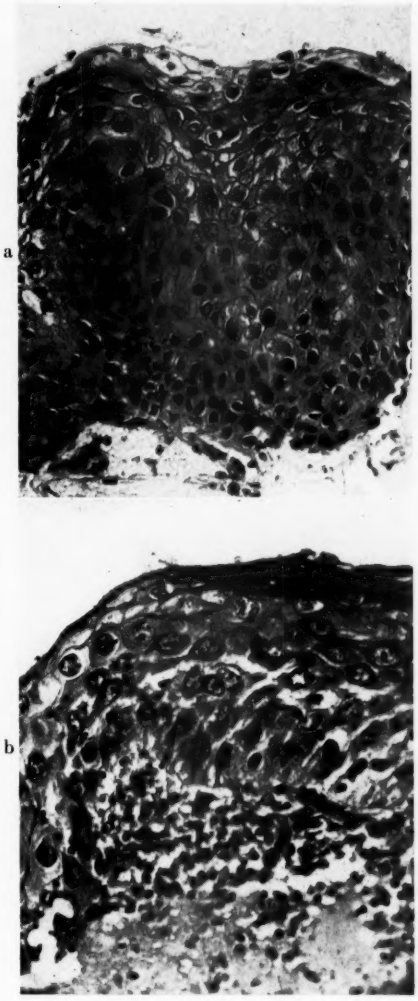


Fig. 5.

Fig. 5. Patient 11. a, NUMS16362. Antepartum biopsy, 17 weeks pregnant. Nuclear abnormalities present in the most superficial layers of the epithelium. Considered an equivocal lesion. ×189. b, NUMS17713. Biopsy at 11 weeks postpartum. The nuclear abnormalities are not present in the superficial layers. Atypical basal cell hyperplasia. ×274.

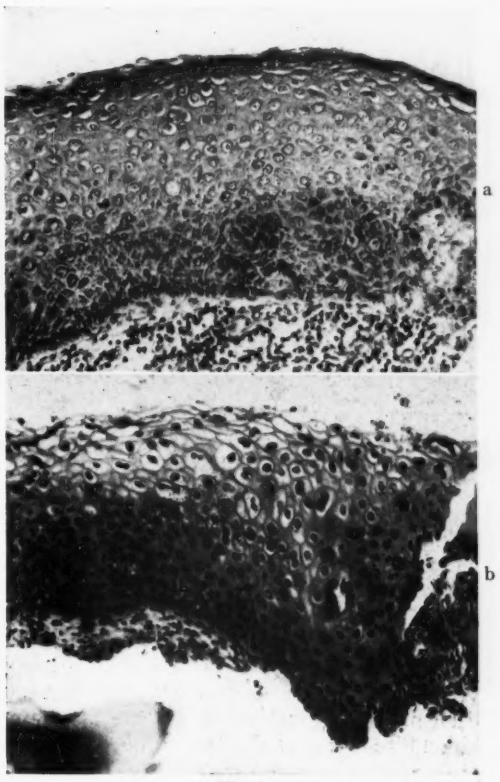
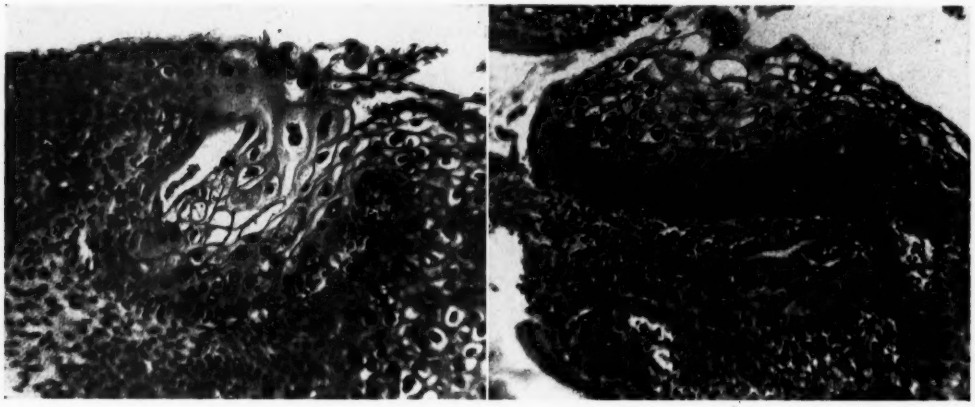


Fig. 6.

Fig. 6. Patient 13. a, NUMS11665. Antepartum biopsy at 31 weeks of pregnancy. Moderate nuclear abnormality and disturbance of polarity are apparent. Considered an equivocal lesion. The superficial layers suggest early hyperkeratinization. ×113. b, NUMS12870. Postpartum biopsy at 37 weeks. Many of the cells appear glycogen-laden although some surface cells have abnormal nuclei. Multiple nuclei are particularly prominent. Also considered an equivocal lesion. ×113.

partum follow-up (11 weeks). Patient 12 is being followed.

In 7 of these patients the lesion persisted (Table II,C). The equivocal lesion has been found in biopsies obtained from 16 to 37 weeks postpartum. In Patient 13 (Fig. 6) following discovery of equivocal lesions in pregnancy and postpartum, the subsequent multiple blocks from the hysterectomy specimen were negative. Patient 14 (Fig. 7) was subjected to biopsy twice during pregnancy (equivocal lesion noted in both) and twice postpartum. Cervical cautery was needed to control bleeding after the biopsy 2 weeks postpartum. In spite of this, the lesion was found 22 weeks postpartum. In Patient 15,



a b

Fig. 7. Patient 14. a, NUMS16040. Antepartum biopsy at the eighth week. Equivocal lesion with bizarre nuclei throughout the epithelium. Vacuolated appearance due to intracellular glycogen removed in fixation. ×131. b, NUMS18025. Twenty-two weeks postpartum. Similar equivocal lesion. Note the resemblance to Fig. 9. ×131.

a biopsy taken at the seventh week postpartum showed a preinvasive carcinoma. Subsequent biopsy at 16 weeks postpartum showed only an equivocal lesion similar to that noted during pregnancy. Subsequently, biopsies have been made at 36 weeks, 1 year, and 3 years and 10 months postpartum; all have been negative. In Patient 16[1] the equivocal lesion discovered at the twenty-ninth week of pregnancy was still present 16 weeks postpartum. A hysterectomy was performed during the twelfth week of a subsequent pregnancy and serial blocks from the cervix revealed a preinvasive carcinoma (Fig. 8).

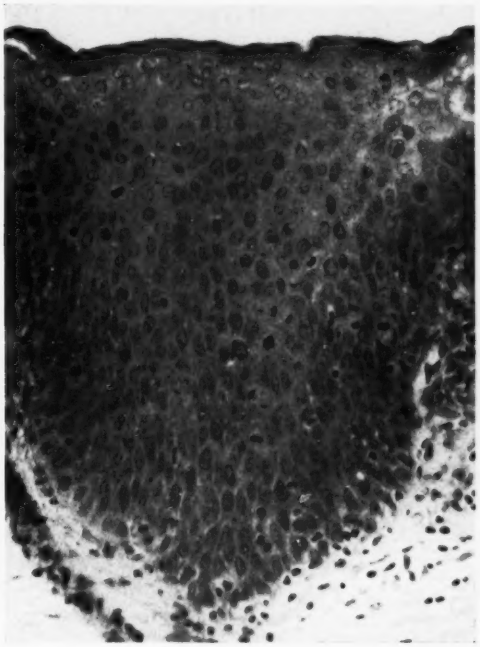
Patient 17 was biopsied on 3 occasions during pregnancy. On 2 of the 3 an equivocal lesion was found. She delivered elsewhere and was not seen again until 12 weeks postpartum following an intervening pregnancy (4 years and 11 months after the first biopsy). Biopsy again showed an equivocal lesion. We interpret this as persistence of the original lesion, since it would seem to be stretching coincidence to expect the original to have disappeared, and the patient to have immediately developed a second such uncommon lesion.

In Patient 18 biopsies made at the thirty-third and thirty-fourth week of pregnancy were interpreted as showing an equivocal lesion (Fig. 9a). Seventeen weeks postpartum a like lesion was found (Fig. 9b). Biopsy 22 weeks postpartum after a subsequent pregnancy again showed an equivocal lesion (Fig. 9c and d).

It is questionable whether the final patient (Table III, No. 20) should be included in this presentation as the original biopsy was made when the patient was not as yet pregnant. We have included this case because we believe that it illustrates the probability that many, if not all, of these lesions as well as our previously reported preinvasive carcinomas, antedated the pregnancy in which they were discovered. Thus, pregnancy in reality is incidental rather than causative (as is implied by the insistence that the lesion to be reported must be discovered during pregnancy). A cervical smear reported as atypical was obtained approximately 8 weeks before conception, and 7 weeks after delivery of her fourth child. A single biopsy was then obtained approximately 1 week before conception (these dates are of necessity vague as the patient was lactating and had not menstruated since her previous delivery 14 weeks prior to biopsy). A minimal atypical basal cell hyperplasia was found. Four quadrant biopsy was repeated 3 to 4 weeks after conception (recorded in the table as 5 to 6 weeks "menstrual" age) and

[1]Patients 10 and 16 were 22 and 16 respectively of a previous report. Pictures of the lesion in Patient 10 appear in that publication (3).

a



b

Fig. 8. Patient 16. a, NUMS12242. Antepartum biopsy at 29 weeks. Mitotic figures were very prominent. Opinion is divided in our laboratory; some consider this lesion atypical metaplasia of endocervical epithelium; others, an equivocal lesion. Sixteen weeks postpartum an equivocal lesion was found. ×66. b, NUMS16308. Hysterectomy specimen obtained at the twelfth week of the next pregnancy. Moderately differentiated preinvasive carcinoma. There are numerous mitotic figures. ×312.

showed an atypical basal cell hyperplasia. Repeat biopsy at the twenty-second week revealed an equivocal lesion (Fig. 10a). Eleven weeks postpartum only a 2 quadrant biopsy was obtained which was negative. The next biopsy was made 8 weeks later before it was recognized that the patient was again about 3 weeks pregnant (ovulation age). This showed preinvasive carcinoma (Fig. 10b). Seventeen weeks after the delivery of her last child the preinvasive carcinoma was again found (Fig. 10c).

Had this patient not been smeared or biopsied prior to the onset of her pregnancy the lesion discovered about 3 to 4 weeks after conception would have been "found in pregnancy." The inference would be drawn by some that pregnancy was responsible despite the fact that this short length of time seems hardly adequate for pregnancy to have accomplished such changes. The same situation existed in the next pregnancy when preinvasive carcinoma was discovered in the fifth week. The findings in this patient seem most easily explained as progression from atypical basal cell hyperplasia to preinvasive carcinoma; the two pregnancies are considered incidental. The likelihood that the preinvasive carcinoma developed as a new lesion during the first 5 weeks of her last pregnancy seems too fantastic to discuss. On the other hand there is a reasonable possibility that the lesion was missed in earlier biopsies.

DISCUSSION

The infrequency with which we have made the diagnosis of atypical basal cell hyperplasia cannot be interpreted as proof of a lower incidence of this lesion in pregnancy than is true for either equivocal lesions or preinvasive carcinoma. Its apparent rarity in our data undoubtedly stems from the method of selec-

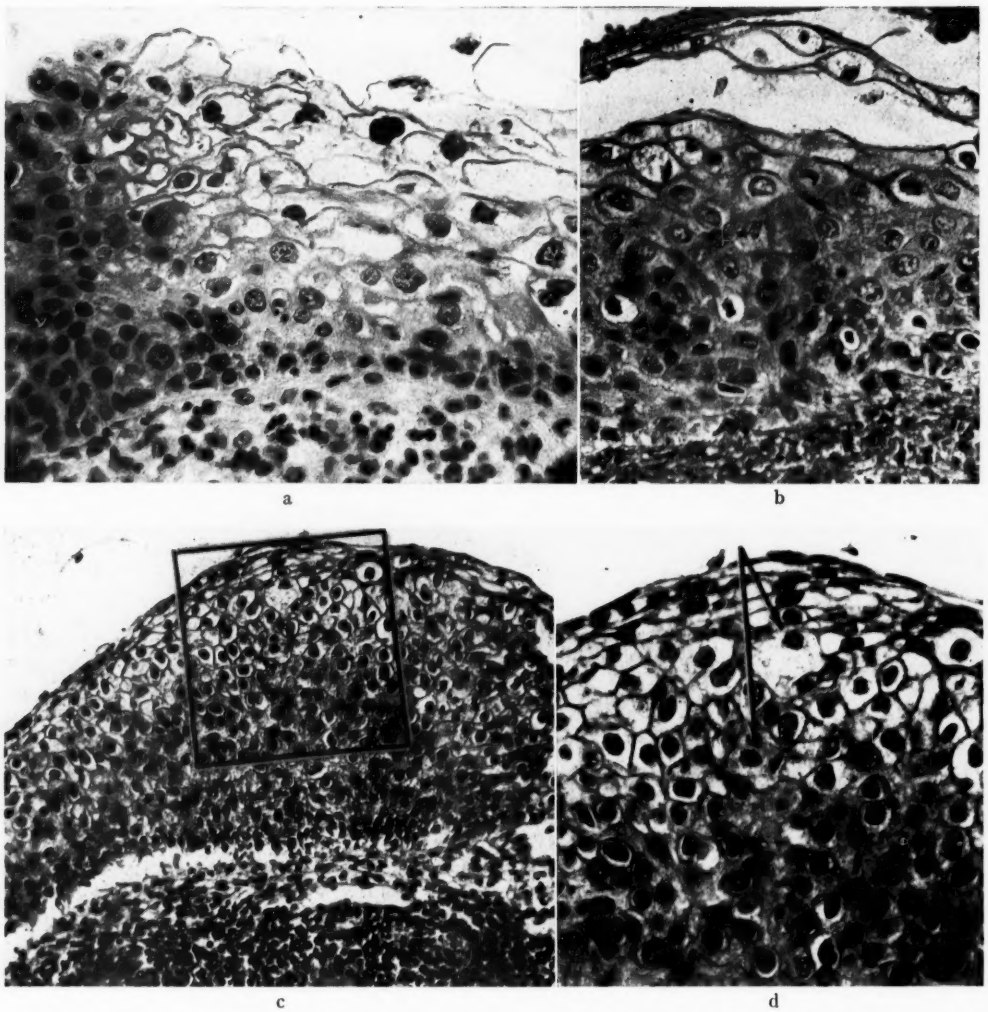


Fig. 9. Patient 18. a, NUMS15432. Antepartum biopsy at 33 weeks of pregnancy. Nuclear abnormalities and partial disturbance of architecture. Many cells appear glycogen-laden; considered to be an equivocal lesion. ×282. b, NUMS16265. Postpartum biopsy at 17 weeks. Similar disorderly arrangement and glycogen deposition. Many mitotic figures, some abnormal; also considered to be an equivocal lesion. ×282. c, NUMS19020. Postpartum biopsy at 22 weeks. Similar equivocal lesion found following a subsequent pregnancy. ×180. d, NUMS19020. Greater magnification of boxed area in Fig. 9c to show mitotic figures (arrows) in superficial layers of this abnormal epithelium. ×350.

tion of patients for biopsy at the Chicago Maternity Center (our largest source of patients). Only those patients with atypical or positive smears, or obvious gross cervical abnormalities have been selected for biopsy because of time and personnel limitations. As may be noted in Table I (and as might be expected from the microscopic appearance of this lesion) the smear or cervical scraping is almost always negative; whereas, with the equivocal lesions, positive or atypical reports were more common. The true incidence of

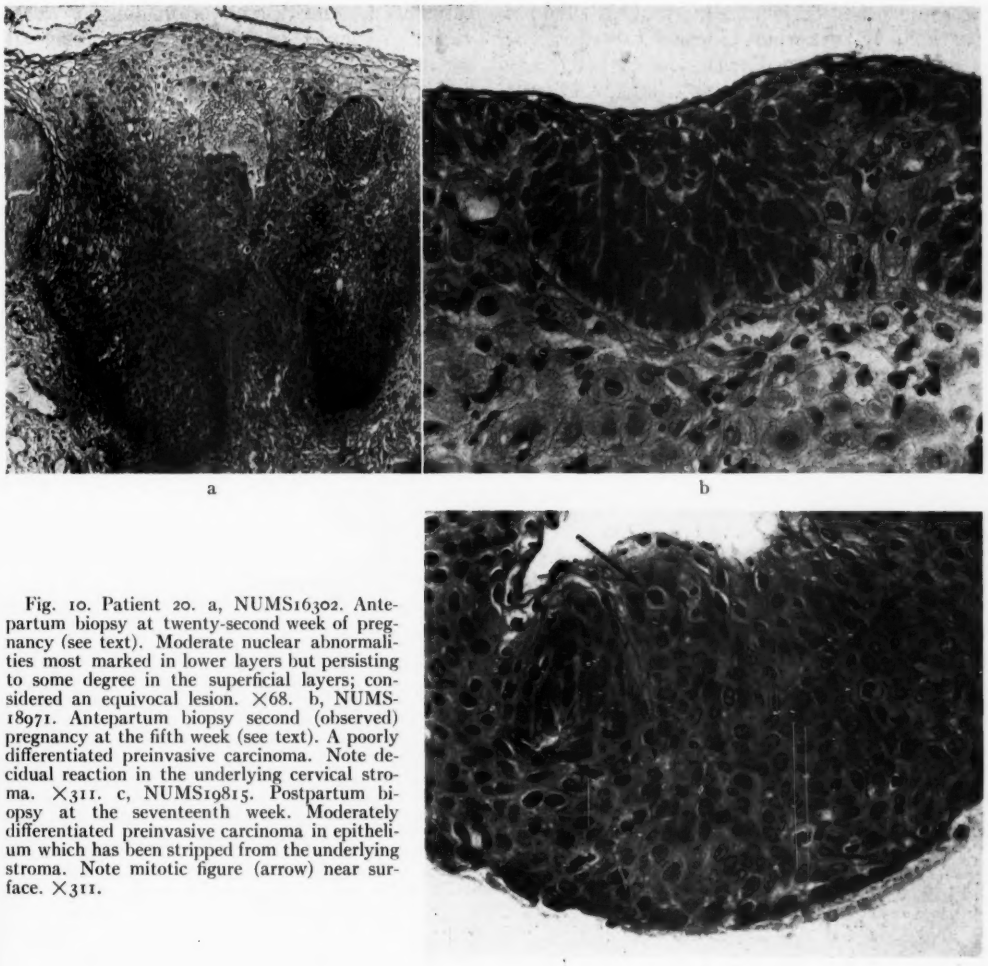


Fig. 10. Patient 20. a, NUMS16302. Antepartum biopsy at twenty-second week of pregnancy (see text). Moderate nuclear abnormalities most marked in lower layers but persisting to some degree in the superficial layers; considered an equivocal lesion. ×68. b, NUMS-18971. Antepartum biopsy second (observed) pregnancy at the fifth week (see text). A poorly differentiated preinvasive carcinoma. Note decidual reaction in the underlying cervical stroma. ×311. c, NUMS19815. Postpartum biopsy at the seventeenth week. Moderately differentiated preinvasive carcinoma in epithelium which has been stripped from the underlying stroma. Note mitotic figure (arrow) near surface. ×311.

any of these lesions during pregnancy can only be determined by unselected sampling; such a study is now being conducted at Cook County Hospital (2) and at the Universitats-Frauenklinik Marburg (U. S. Zone) Germany (6). This lesion (atypical basal cell hyperplasia) is apparently more common than either equivocal lesions or preinvasive carcinoma, when the patients biopsied are unselected.

To some it may appear startling that 5 of the 14 equivocal lesions apparently disappeared (35.7 per cent). However, such a disappearance rate postpartum is approximately the same as that which occurs with similar lesions in patients who are not pregnant. In a series of 41 nonpregnant patients with equivocal lesions, followed in our laboratory, the lesion apparently disappeared in 13 or 31.7 per cent. Undoubtedly, the difference between 35.7 and 31.7 per cent is not significant. It is dangerous to assume that a lesion has necessarily regressed or disappeared, because a subsequent biopsy is negative after an earlier one had contained an equivocal lesion

or some other cervical abnormality. This is particularly true when biopsies are not of the 4 quadrant variety. Further, even though the hysterectomy or cone amputation specimen is found to be negative, after serial blocking or even after serial sectioning (though this is usually not practical), that too cannot be presented as definite proof of regression, particularly when there have been repeated biopsies and/or cone excisions or amputations previously. When a hysterectomy is performed within a month after a positive biopsy, it would seem unlikely that sufficient time had elapsed for regression to occur. Nevertheless, in 13.5 per cent (8 of 59) of such patients with preinvasive carcinoma, the lesion could not be found in our own surgical specimens (7). The reasons for these disappearances are probably multiple. Judging from the fact that the likelihood of disappearance increases as the size of the lesion decreases as determined by 4 quadrant biopsy (its presence in 1, 2, 3, or 4 quadrants) the destruction of the lesion by biopsy and/or the accompanying inflammatory response to such trauma is a significant possibility in small lesions. When a lesion has persisted for 6 months postpartum, in spite of repeated biopsies and even a cone amputation, only to apparently disappear on serial blocking of the hysterectomy specimen obtained 7½ weeks after the last biopsy, as in Mullen and Foraker's case, a word of comment is needed not because it had apparently disappeared but rather because it had survived so long despite so much previous diagnostic and therapeutic trauma to the cervix.

In recent years our diagnostic criteria for preinvasive carcinoma of the cervix have become more conservative. In the years 1949, 1950, and 1951 several of the patients with lesions which we now consider equivocal were subjected to hysterectomy. Obviously, these patients were overtreated, because at that time the lesion was believed to be preinvasive carcinoma.

SUMMARY AND CONCLUSIONS

Nineteen patients with abnormalities (not preinvasive carcinoma) of the cervical squamous epithelium discovered in biopsies taken during pregnancy have been followed through one or more pregnancies and well into the postpartum period. Five had an atypical basal cell hyperplasia of the squamous epithelium. In the remaining 14 patients the lesions were considered equivocal (i.e. the criteria were insufficient for a diagnosis of preinvasive carcinoma but the abnormality was more extensive than in an atypical basal cell hyperplasia). In 4 of the 5 patients with an atypical basal cell hyperplasia, the lesion persisted from 12 to 28 weeks postpartum. In 1 the lesion could not be found following the termination of pregnancy. Of the 14 equivocal lesions followed, 7 persisted (from 12 to 37 weeks postpartum), 2 apparently regressed to a basal cell hyperplasia and 5 could not be found following the termination of pregnancy. In an additional patient, atypical basal cell hyperplasia was discovered about 1 week prior to conception. This apparently progressed to preinvasive carcinoma in a period of 3 years (and 2 pregnancies).

The significance of these observations is discussed. We believe that these lesions of the cervix are incidental findings during pregnancy; we do not believe that they are a specific pregnancy change of the squamous epithelium.

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THE INFLUENCE OF STASIS ON BONE GROWTH

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THE many experimental attempts to stimulate longitudinal bone growth are evidence that no simple, satisfactory method has been found. Most methods are based upon the premise that increased local arterial hyperemia acts as a stimulus to the epiphysis. In all of the conditions in which increased longitudinal bone growth has been observed, e.g., congenital arteriovenous aneurysms, fracture of the shaft of long bones, and osteomyelitis, this arterial hyperemia has been assumed to be the common factor. However, stasis is a factor common to these conditions and has received little attention. In a previous work (3), the authors have shown that the changes of stasis occur in bones distal to an area of trauma. It may be that all previous attempts at stimulation of longitudinal bone growth by drilling or by placing screws, ivory pegs, wires of dissimilar metals, and chemicals near the epiphysis have succeeded or failed according to the degree of stasis which the method produced. This would account for many of the variable results reported. The following experiments were undertaken in an attempt to determine the effects of stasis upon growing bone.

PROCEDURE

Tourniquets. Foreleg tourniquets.—In 11 growing mongrel dogs of estimated age under 3 months, tourniquets were applied around the left forelegs just below the elbows. This was found to be the most efficient place, since tourniquets applied above this level soon cut into the skin and muscles. A disadvantage of below-elbow tourniquets was that only one epiphysis of the radius and ulna was affected.

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Through trial and error, the following tourniquet was evolved. A layer of elastic adhesive bandage was placed next to the skin. Over this, a few turns of rubber reinforced bandage were applied, followed by a few more turns of elastic adhesive. With reasonable care, a moderate degree of edema of the leg distal to the tourniquet was maintained without damage to the skin. Edema was constantly present in most of the animals, and even when not constant, it was never absent for more than 2 days. These animals were sacrificed at intervals between 18 and 132 days.

Hindleg tourniquets.—In 6 growing dogs under 3 months of age, tourniquets similar to those described were applied to the left hindlegs above the knee joints. Since stasis affected all epiphyses distal to the tourniquets, more epiphyses were involved than in the foreleg experiments. These dogs were sacrificed at intervals between 25 and 75 days.

Roentgenograms of all bones were made prior to measurement. The bones of the forelegs and hindlegs were then removed and measured. The volume of the bones after stripping off all soft tissues and periosteum was determined by submerging them in a water filled graduate and measuring the displaced water. Midsagittal sections were taken in some instances from the distal radius, femur, or tibia for microscopic examination of the epiphysis and periosteum. In all experiments, the opposite comparable extremities served as controls.

In many instances, the data appear incomplete because of the fact that volume determinations and microscopic sections could not be obtained from the same bone, since the soft tissues had to be stripped for accurate volume determination, yet for the microscopic sections it was desirable to leave the soft tissues intact for study of the periosteum.

It was found that accurate longitudinal measurements of the bones could not be made

TABLE I.—TOURNIQUET STASIS OF FORELEGS

Dog No.	Procedure	Duration of edema in days	Length of radius in inches		Radius length difference in inches	Per cent difference in radius length	Radius proximal diameter measured 1 inch from proximal end		Radius proximal diameter difference in inches	Radius distal diameter measured 45/64 inch from distal end		Radius distal diameter difference in inches	Per cent difference in radius distal diameter	Volume of radius, c.c.		Per cent volume increase of radius
			Left	Right			Left	Right		Left	Right			Left	Right	
11	Tourniquet, left foreleg	132	5 29/64	5 22/64	2/64 Decrease	0.6 Decrease	22/64	22/64	0	28/64	26/64	2/64 Increase	7.7 Increase	9.25	8.50	8.8
14	Tourniquet, left foreleg (theelin)*	40	4 4/64	4 2/64	2/64 Increase	0.8 Increase	20/64	20/64	0	30/64	26/64	4/64 Increase	15.4 Increase			
16	Tourniquet, left foreleg (testosterone)*	94	4 40/64#	4 36/64#	4/64 Increase	1.4 Increase	21/64	21/64	0	28/64	24/64	4/64 Increase	16.6 Increase			
17	Tourniquet, left foreleg	64	4 53/64#	4 50/64#	3/64 Increase	1.0 Increase	21/64	21/64	0	30/64	28/64	2/64 Increase	7.2 Increase			
18	Tourniquet, left foreleg	75	4 41/64#	4 42/64#	2/64 Increase	0.67 Increase	21/64	21/64	0	34/64	30/64	4/64 Increase	13.3 Increase			
19	Tourniquet, left foreleg	18	3 51/64#	3 52/64#	2/64 Increase	0.85 Increase	21/64	21/64	0	36/64	32/64	4/64 Increase	11.1 Increase			
21	Tourniquet, left foreleg	38	3 26/64#	3 21/64#	2/64 Increase	0.93 Increase	20/64	20/64	0	28/64	24/64	4/64 Increase	16.6 Increase			
22	Tourniquet, left foreleg	38	4 35/64	4 35/64	None		31/64	31/64	0	44/64	40/64	4/64 Increase	10.0 Increase			
23	Tourniquet, left foreleg	38	5 7/64	5 9/64	2/64 Decrease	0.60 Decrease										
25	Tourniquet, left foreleg; epiphyses closed	26	4 22/64	4 26/64	4/64 Decrease	1.4 Decrease	25/64	25/64	0	28/64	24/64	4/64 Increase	16.6 Increase	7.0	6.0	16.6 Increase
8	Tourniquet, left foreleg	36	5 50/64#	5 41/64#	9/64 Increase	1.65 Increase	32/64	32/64	0	32/64	29/64	3/64 Increase	10.3 Increase			

Radius length—average increase 1.04 per cent (for all increased)
Radius diameter distal—average increase 12.48 per cent
Radius volume—average increase 12.7 per cent
#Sections taken for microscopic examination
*Received daily injections of these as part of another experiment, but since both animals showed changes they are included

from the roentgenograms. All longitudinal measurements were accurately done on the grossly dissected bones. The transverse diameter of each radius was determined by measurement 1 inch below the radial head and ¾ inch proximal to the radial styloid. Most measurements were made with a Vernier caliper.

Transverse drilling of the distal metaphysis of the left femur. In 10 growing dogs, the lateral surface of the left femur was exposed through a small incision, and a ¼ inch diameter hole was drilled through the femur approximately 1 inch proximal to the distal epiphysis. The wounds healed promptly and the animals continued to use the extremities normally. The animals were sacrificed at intervals between 16 and 140 days postoperatively, and the overall lengths of the femora were measured accurately with a Vernier caliper. Histologic sections were prepared and studied. Some animals had a second and third drilling at the same site (Table III).

RESULTS

Tourniquets. Foreleg tourniquets (see Table I for data on individual animals).—All forelegs to which tourniquets were applied showed an increase in transverse diameter of the distal half of the radius which averaged 12.5 per cent as compared with the control radius. In all animals, the proximal half of the radius above the tourniquet showed no change as compared with the control radius. The volume was determined in only 2 animals, but these showed an average increase of 12.7 per cent of the left radius. Increase in length was less constant than increase in diameter. Seven of the 11 animals showed increase in length of the radius and this increase averaged 1.04 per cent. One

TABLE II.—TOURNIQUET STASIS HINDLEGS

Dog No.	Procedure	Duration of edema in days	Length of femur in inches		Femur length difference in inches	Per cent difference in femur length	Length of tibia in inches		Tibia length difference in inches	Per cent difference in tibia length	Volume of tibia, c.c.		Per cent volume increase of tibia
			Left	Right			Left	Rigth			Left	Right	
17	Tourniquet, left hindleg	47	$5\frac{18}{64}$	$5\frac{18}{64}$	$\frac{0}{64}$	No difference	$5\frac{34}{64}$	$5\frac{32}{64}$	$\frac{11}{64}$ Increase	3.5 Increase	17.5	14.0	25 Increase
21	Tourniquet, left hindleg	37	$3\frac{49}{64}$	$3\frac{47}{64}$	$\frac{2}{64}$ Increase	0.8 Increase	$3\frac{39}{64}$	$3\frac{45}{64}$	$\frac{6}{64}$ Increase	1.7 Increase	10.0	9.5	5.55 Increase
22	Tourniquet, left hindleg	25	$5\frac{0}{64}$	$5\frac{0}{64}$	$\frac{0}{64}$	No difference	$5\frac{14}{64}$	$5\frac{10}{64}$	$\frac{4}{64}$ Increase	1.2 Increase	18.5	17.5	5.71 Increase
23	Tourniquet, left hindleg	38	$5\frac{7}{64}$	$5\frac{49}{64}$	$\frac{2}{64}$ Increase	0.55 Increase	$5\frac{50}{64}$#	$5\frac{46}{64}$#	$\frac{4}{64}$ Increase	1.1 Increase			
25	Tourniquet, left hindleg	26	$4\frac{54}{64}$	$4\frac{54}{64}$	$\frac{0}{64}$	No difference	$4\frac{62}{64}$	$4\frac{60}{64}$	$\frac{2}{64}$ Increase	0.63 Increase			
18	Tourniquet, left hindleg	75	$5\frac{60}{64}$#	$5\frac{56}{64}$#	$\frac{4}{64}$ Increase	1.8 Increase	$5\frac{12}{64}$	$5\frac{10}{64}$	$\frac{2}{64}$ Increase	0.59 Increase	16.5	15.0	3.33 Increase

Femur length—average increase 0.52 per cent (for all increased)
Tibia length—average increase 1.45 per cent
Tibia volume—average increase 7.91 per cent
#Sections taken for microscopic examination

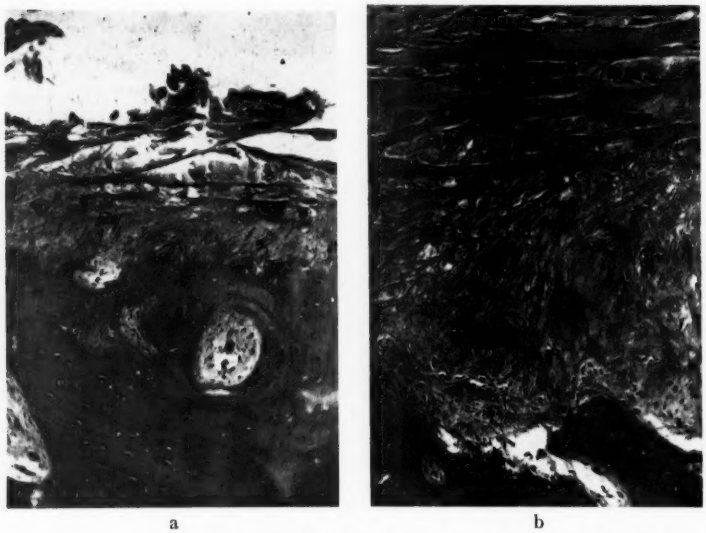
TABLE III.—TRANSVERSE DRILLING OF THE DISTAL FEMORAL METAPHYSIS

Dog No.	Left lower femur drilled	Repeat drilling	Days total time	Femur length in inches		Difference in length in inches	Per cent difference in length	Tibia length in inches	
				Left	Right			Left	Right
1	11-13-51	1- 4-52	21	$3\frac{56}{64}$#	$3\frac{54}{64}$#	$\frac{2}{64}$ Increase	0.81 Increase		
2	11-13-51		16	$3\frac{42}{64}$#	$3\frac{40}{64}$#	$\frac{2}{64}$ Increase	0.86 Increase		
3	11-13-51		25	$3\frac{19}{64}$#	$3\frac{18}{64}$#	$\frac{1}{64}$ Increase	1.0 Increase		
4	11-20-51		16	$4\frac{18}{64}$	$4\frac{18}{64}$	None	—		
6	11-20-51	12-10-51 1- 4-52	98	$4\frac{53}{64}$#	$4\frac{51}{64}$#	$\frac{2}{64}$ Increase	0.65 Increase		
7	12-10-51		120	$4\frac{4}{64}$	$4\frac{4}{64}$	None	—		
8	12-10-51	1- 4-52	140	$6\frac{30}{64}$#	$6\frac{34}{64}$#	$\frac{4}{64}$ Decrease	0.82 Decrease		
9	12-10-51	1- 4-52	38	Approx. $5\frac{52}{64}$	$5\frac{50}{64}$	$\frac{2}{64}$ Increase	0.54 Increase		
13	1-19-52		38			None			
16	1-19-52		103	$5\frac{14}{64}$	$5\frac{19}{64}$	$\frac{5}{64}$ Decrease	1.5 Decrease	$4\frac{56}{64}$	$4\frac{51}{64}$

Average increase—0.77 per cent for those showing increase
Average decrease—1.2 per cent for those showing decrease
#Sections taken for microscopic examination

radius showed no difference in length, although there was a 10 per cent increase in volume. Three animals showed a decrease in length of the experimental legs. Two of these had open epiphyses, and the decrease in the length of the radii amounted to 0.6 per cent each. The third animal, showing a 1.4 per cent decrease in length of experimental radius, had closed epiphyses, but radial volume and diameter were increased 16.6 per cent over control.

Hindleg tourniquets (see Table II for data on individual animals).—All hindlegs to which tourniquets were applied showed an increase in length and diameter of the tibiae (Fig. 4). The average increase in length was 1.45 per cent and the average increase in volume was 7.9 per cent. The changes in the femora were less constant, with only one-half showing an increase in length, averaging 0.52 per cent. The other half showed no difference in length.



a b

Fig. 1. a, Photomicrograph (× 55) of section from distal right radius of dog 16 showing bone and periosteum. b, Photomicrograph (× 55) of section from distal left radius of dog 16 following tourniquet stasis of 94 days, showing bone and periosteum. Note the increase in cellularity and thickness of the periosteum as compared with the control.

The difference in length and diameter of the bones of the foot were too slight for accurate measurement in all but 1, which showed 1.4 per cent increase in length of the metatarsals in the experimental leg.

Transverse drilling of the distal metaphysis of the femur (see Table III for data on individual animals). The results of lower femoral stimulation by drilling were inconsistent as have been the results of others attempting stimulation by various procedures.

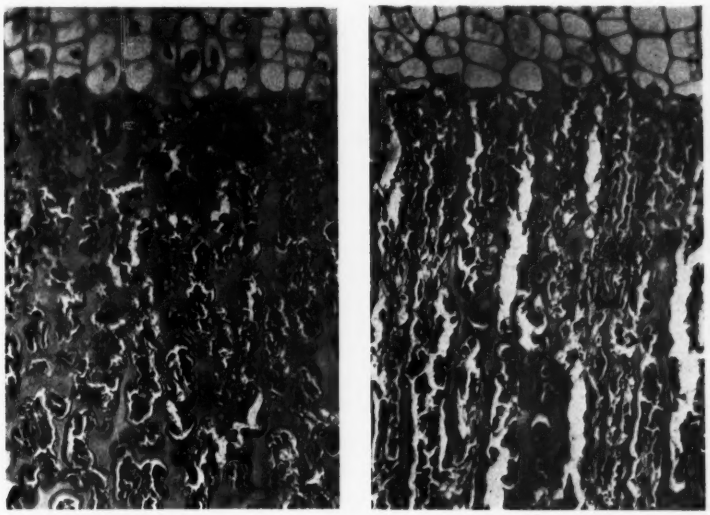
Only 5 of the 10 animals showed an increase in length, and this increase averaged 0.77 per cent. Three animals showed no difference in femoral length, and 2 animals showed decrease of femoral length averaging 1.2 per cent on the experimental side.

Microscopic findings. The microscopic changes in all bones following stasis and the trauma of metaphyseal drilling were the same, although following metaphyseal drilling, the changes were less marked.

The experimental bones showed marked thickening of the periosteum with increased cellularity, but no evidence of increased vascularity. The outer boundary of the subperiosteal bone was less well defined as compared with the control, and there was less definite cortex formation (Fig. 1). No difference in thickness of the uncalcified epiphyseal cartilage was noted.

In the process of enchondral longitudinal bone growth, there is vascular invasion of the zone of calcified cartilage with the formation of calcified cartilaginous trabeculae. In the control sections, this zone of calcified cartilage is incompletely invaded with vascular tissue and appears as a sheet of cartilage containing numerous irregular vascular channels (Fig. 2a). In the experimental sections, vascular invasion of the calcified cartilage zone is more complete with the formation of long thin parallel cartilaginous trabeculae, with a greater amount of vascular connective tissue between the formed trabeculae (Fig. 2b).

As the zone of calcified cartilage is eroded and trabeculae are formed, new bone appears on the surfaces of the trabeculae. In the control sections, this process of ossification of the trabeculae occurs at some distance from the epiphyseal line since there is a sheet of incompletely vascularized calcified cartilage be-



a b

Fig. 2. a, Photomicrograph (× 90) of section from distal right radius of dog 18 showing normal zone of calcified cartilage. b, Photomicrograph (× 90) of section from distal left radius of dog 18 following tourniquet stasis of 75 days. Note the more complete erosion of calcified cartilage with formation of long, thin cartilaginous trabeculae. There is bone apposition near the epiphyseal line.

tween the cartilaginous trabeculae and the epiphyseal line. In the experimental sections, bone apposition is seen much nearer the epiphyseal line, and frequently immediately adjacent to it, since well formed cartilaginous trabeculae are present at the epiphyseal line. The thin, long primary bony trabeculae of the experimental sections persist, giving the bone a porous structure, while in control sections the bony trabeculae become thicker and more irregular in the process of forming normal cancellous bone.

DISCUSSION

These experiments have shown that increased growth in both length and width of bone occurs following stasis distal to a tourniquet. Increase in longitudinal growth was less constant in the forelegs in our experiments than in the hindlegs, possibly because fewer epiphyses were stimulated by the foreleg tourniquets which were placed below the elbows. In all radii and tibiae, the increase in diameter was proportionately much greater than the increase in length. This increase in diameter was present even in those bones which showed no increase in longitudinal growth. In the radii, the increase in diameter began at the level of the tourniquet and extended distally to the epiphysis (Fig. 3). The distribution and contour of this increased diameter indicate that it is the result of subperiosteal new bone proliferation and is not entirely due to failure of absorption or remodeling since the longitudinal growth over the period of time of the experiment would be only a few millimeters. The bone assumes a more cylindrical shape with less flare of the metaphyses due to this increase of bone diameter.

It has been stated that a marked secondary arterial hyperemia follows release of a tourniquet. In these experiments, this arterial hyperemia was largely eliminated by the maintenance of near constant edema for the duration of the experiment, and it was thought that stasis was the factor present responsible for the increase in growth.

The stimulation of longitudinal bone growth by stasis is not a new concept, but there has been insufficient experimental data produced on the subject; and the few clinical trials in which it was used have been forgotten.

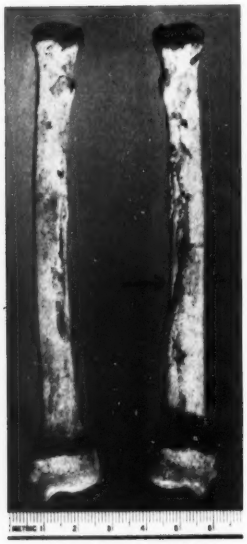


Fig. 3. Photograph of both radii of dog 11 following tourniquet stasis of 132 days. Although there was not an increase in longitudinal growth in this particular animal, there is still the typical increase in diameter of the left radius distal to the tourniquet site indicated by the arrows. No increase in diameter of the left radius is noted proximal to the tourniquet.

In 1936, Kishikawa, of Japan, produced increased bone growth in rabbits by placing rubber bands around the extremities. Data were not given as to the number of animals used or the exact results found. Dumreicher, Thomas, and Helfrich, as cited by Schuller and Bier, stimulated bone growth by an elastic tourniquet. Schuller, in 1889, used tourniquets to treat 2 patients with shortened lower extremities following poliomyelitis, and in 1, obtained 1 centimeter growth in 3 months. Servelle, 1948, studied 14 patients who had varices dating from childhood as a result of compression of the femoral or popliteal veins and, in all cases, found increase in length of the affected extremity, although he reported no increase in diameter of the diaphyses as compared to the normal side.

In 7 dogs, Servelle found that deep vein ligation resulted in increased bone growth of the femora and tibiae. He suggested that leg length difference in children could be corrected either by vein ligation or by production of arteriovenous aneurysms in the shortened extremity.

Janes and Musgrove produced marked overgrowth of bones in growing dogs by the surgical production of arteriovenous aneurysms of the iliac vessels. The venous pressure is increased in arteriovenous aneurysms resulting in stasis which, in the authors' opinion, is the cause of this increased growth rather than an increase in arterial blood flow, as suggested by Janes and Musgrove.

Stasis produces biochemical and histologic changes, such as increased protein concentration, increased oxygen availability, and cellularity of periosteum, characteristic of inflammation. This may adequately explain the increased bone growth produced by stasis. The difference in the effect of stasis upon growing and adult bone probably lies in the difference in osteogenetic potency of the periosteum and epiphyses. The authors have shown that in adult bone, stasis produces subperiosteal bone absorption resulting in osteoporosis, whereas, in growing bone, stasis produces porous subperiosteal bone proliferation and epiphyseal changes previously described. In both growing and adult bone, there is marked increase in cellularity of the periosteum.

Conflicting results have been obtained by attempts to stimulate longitudinal bone growth by sympathectomy which many assume to cause a vascular condition opposite that of stasis.

Bone and its related structures have suffered almost every conceivable type of trauma in attempts to find a method to consistently stimulate longitudinal bone growth. Wu and Miltner, Compere and Adams, and Pease have adequately reviewed the many experimental techniques. All methods produced trauma to the bone, and in many increase in width as well as length of bone was also observed. Pease and Blount have noted increased growth of the tibiae following lower femoral stimulations. Blount also states that the trauma of removal of femoral staples in itself is a stimulus to bone growth. The authors believe that in these examples the growth increase in the distal bones is due to stasis resulting from trauma.

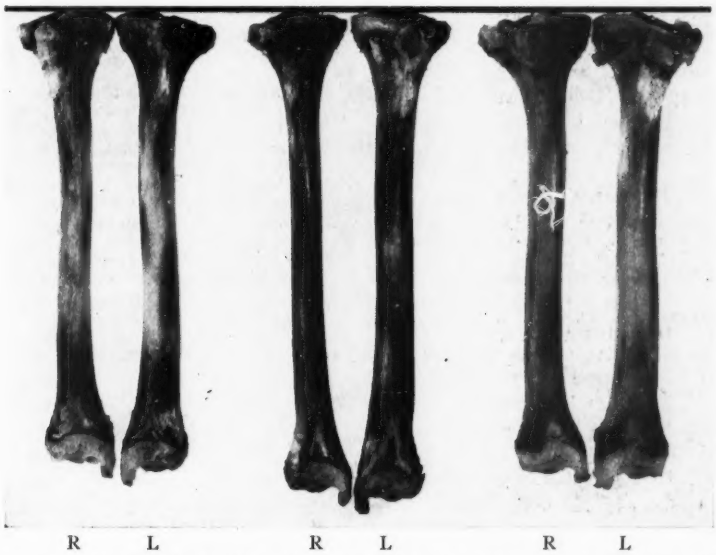


Fig. 4. Photograph of right and left tibia of dog 18, following tourniquet stasis of 75 days on the left; dog 17, following tourniquet stasis of 47 days on the left; and dog 22, following tourniquet stasis of 25 days on the left. Each left tibia shows an increase in length and diameter compared with its control right tibia.

Epiphyseal stimulation by the trauma of transverse drilling of the distal femoral metaphysis results in a microscopic picture, distal to the trauma, identical in character but less in degree with that produced by stasis. There is thickening of the periosteum and increased cellularity with trabecular changes similar to those produced by stasis. Trauma produces interruption of blood vessels, hemorrhage, reactive edema, and callus formation which partially blocks venous return distal to the traumatized area. Stasis produced by tourniquet and trauma to bone (in the form of epiphyseal stimulation) has the same effect on all distal epiphyses. The similarity of microscopic changes is evidence to indicate that the trauma of stimulation produces stasis which stimulates longitudinal bone growth. In 1 instance, the tibia distal to the transverse drilling procedure was measured; and in that case, there was increase in tibial length on the experimental side.

The many methods of epiphyseal stimulation have not consistently produced increased longitudinal growth, and occasionally have resulted in a shorter extremity. Our results in experimental epiphyseal stimulation with trauma have also been inconsistent. Tourniquet stasis, on the other hand, has consistently produced an increase in longitudinal bone growth in all hindlegs. Over half the forelegs grew longitudinally after stasis.

In view of this experimental evidence, a clinical trial of stimulation of longitudinal bone growth by a tourniquet seems warranted. Such clinical studies are in progress.

CONCLUSIONS

1. In growing bones distal to a tourniquet which produces stasis, there is consistent stimulation of growth in width.

2. Increase of growth in length of bones was less constantly produced by stasis except when two epiphyses of one bone were present distal to the tourniquet, as in the tibiae.

3. Bone trauma in the form of transverse drilling of the distal femoral metaphysis gives inconsistent stimulation of longitudinal bone growth. The results are similar to other types of surgical epiphyseal stimulations.

4. The microscopic appearance of bone, epiphyses, and periosteum distal to an area of trauma or a tourniquet are similar.

5. It is believed that the success of all methods designed to stimulate longitudinal bone growth depends on the degree of stasis produced.

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DISTAL INTRAMURAL SPREAD OF CARCINOMA OF THE RECTUM AND RECTOSIGMOID

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THERE has been considerable controversy among surgeons as to the choice of operation for carcinomas of the upper rectum and rectosigmoid. This area is approximately that portion of the bowel lying between 5 to 18 centimeters from the dentate line. The choice lies between an abdominoperineal resection on the one hand and anterior resection or some other type of sphincter-saving procedure on the other. The question is whether or not the less radical procedures can offer the patient as good a chance of cure without sacrifice of the anal sphincter as the more radical operation.

The answer must depend largely on a better understanding of the lymphatic and venous spread of these tumors. It must depend on accurate information as to: (1) the danger of local implantation of tumor cells in a low anastomosis in the rectum, (2) lateral lymphatic spread, (3) extramural retrograde spread to the nodes, and (4) intramural retrograde spread in the bowel wall.

The danger of implanting tumor cells in the suture line or in any adjacent raw area when a low anastomosis is done has been recently emphasized by Goligher and also by Cole. Such a possibility is of course avoided in abdominoperineal resection unless the rectum is perforated during the dissection. Goligher found local recurrences in 16, or 10 per cent of 162 patients who had had resection of the proximal rectum followed by end-to-end anastomosis or colostomy and inversion of the rectal stump (Hartmann operation). In 10, or 6.1 per cent, the recurrence occurred at the suture line or at the site of inversion and was believed to have been caused by local implantation of cancer cells. In 55 patients similarly treated, Cole found local recurrences in 9, or 16 per cent. Six occurred at the suture line, an incidence of 10.9 per cent.

Lateral lymphatic spread occurs almost entirely in tumors of the rectum lying beneath the pelvic peritoneum. It is probably of lesser importance than the upward inferior mesenteric route and is most often found when the upward lymphatics are blocked. The lymphatics follow the middle hemorrhoidal vessels to the iliac and hypogastric nodes, and also pass by other channels posteriorly to the sacral nodes and anteriorly to the tissues about the bladder, prostate, and vagina. The question as to whether cancer spreading along these routes can be removed as effectively by anterior resection as by abdominoperineal resection is still open to debate and will not be discussed in this report.

Extramural retrograde spread to lymph nodes lying distal to the tumor has been studied by many investigators. Most of these studies have shown that such extension is rare, is usually limited in extent, and occurs only when the lymphatics draining upward in the bowel wall are blocked by node metastases. In 1946, Glover and Waugh, after careful study of 100 advanced tumors of their own and a review of others similarly studied and reported in the literature, found an incidence of distal spread to the nodes of only 1 per cent. More recently Dukes found distal spread to the nodes in 6.5 per cent of 1,500 specimens of rectal cancer removed by abdominoperineal resection. In 4.5 per cent the involved nodes lay within ¼ inch of the tumor. In only 2 per cent of the cases were the metastases ¾ inch or more below the tumor.

Intramural distal spread in the wall of the bowel may prove to be as important as, if not more so than, extramural extension. Until recently it has not received sufficient atten-

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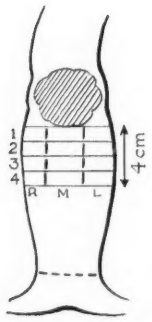

Fig. 1. Method by which blocks of tissue were taken below the tumor for sectioning.

tion. From combined studies of both these paths of spread the surgeon should be better able to judge how great a margin of uninvolved bowel he must remove below the tumor. This has been the purpose of this report.

HISTORICAL REVIEW

In 1910 Handley reported a case of carcinoma of the rectum with evidence of lymphatic permeation in the bowel wall for 5 inches above and below the lesion. Winkler also believed such extension could occur for 8 centimeters proximally and distally. Others, however, questioned their findings. Most observers, starting with Clogg in 1904 and followed by Cripps, Cole, Wood and Wilkie, Westhues, Gordon-Watson, Dukes, Glover and Waugh, and Black and Waugh have agreed that intramural spread is insignificant and that resections of the bowel can be carried out safely within a few centimeters of the tumor.

In 1949, however, Connell and Rottino reported retrograde intramural spread in 4 of 9 cases of cancer of the rectum and rectosigmoid studied by a modified serial section technique of the circumference of the bowel. In these 4 specimens distal tumor spread was found at distances of 7, 4.2, 4.1, and 5.2 centimeters, respectively, below the lower margin of the primary tumor. Data on the presence of lymph node metastases were given in only 1 case. In this case none was found.

Recently, Quer, Dahlin, and Mayo reported 93 specimens of cancer of the rectum and rectosigmoid lying from 5 to 15 centimeters inclusive above the dentate line which were studied by multiple sections of the bowel taken below the tumor at intervals of 5 millimeters. Specimens were consecutive except that only those removed at operations believed to be curative were studied. They concluded that a margin of 2.5 centimeters of uninvolved bowel below the tumor is sufficient in tumors of low grade malignancy (Broders' grade 1 or 2) and that a margin of 6 centimeters or more should be allowed in lesions of high grade malignancy (Broders' grade 3 or 4). As only 3 of 91 patients had evidence of distal extension beyond 1.5 centimeters and 86 had none whatever, they believed that this avenue of tumor spread did not present a problem in the management of operable tumors.

MATERIALS AND METHODS

One hundred and twenty-six operative specimens of carcinoma of the lower colon and rectum were studied. Nearly all specimens were consecutive except in a few instances and in these no selection of specimens was made. Measurements were obtained from the gross pathologic material and from proctoscopic examination. The specimens included those removed by either abdominoperineal, anterior, or sigmoid resection. In the specimens removed by anterior or sigmoid resection only those with at least 3 centimeters of bowel wall below the tumor were included.

Each specimen was examined immediately after operation. Measurements were taken and a drawing of the specimen was made. It was then pinned out on a cork board to prevent shrinkage and placed in 10 per cent formalin for 24 to 48 hours. Blocks of tissue were then cut approximately 1 centimeter in width through the bowel wall distal to the tumor at right angles to the axis of the bowel. At least 3 blocks were cut distal to the lesion for a distance of at least 3 centimeters, but usually of 4 centimeters or more, and were then divided into 2 or 3 parallel rows, depending on the width of the specimen. Occasionally they were taken over a distance of 8 to 9 centimeters. After they were imbedded in paraffin, 4 sections were taken from the upper surface of each at intervals of 250

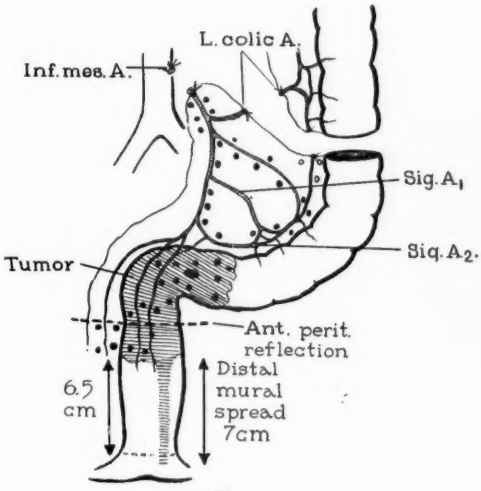

Fig. 2.

Fig. 2. Case 1. A carcinoma of the rectosigmoid removed by palliative abdominoperineal resection with ligation of the inferior mesenteric artery at the aorta. Metastases were present in 63 of 67 nodes in the cleared specimen. In addition to lateral spread along the paracolic lymphatics of about 15 centimeters, there was distal mural spread of 7 centimeters to below the dentate line.

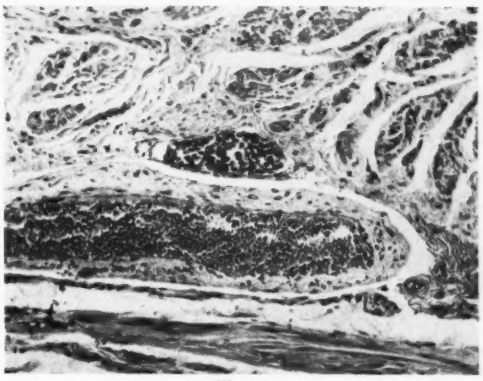

Fig. 3.

Fig. 3. Case 1. Perivascular lymphatic filled with tumor cells 6.5 centimeters below the tumor. ×97.

microns. They were then stained with hematoxylin and eosin for microscopic examination. If further sections were desired they were cut at intervals of 250 to 500 microns through the remainder of the block. The average number of sections per specimen was 42. In a few instances when retrograde spread was found many more sections were cut. In 1 specimen 296 sections were taken. Over 5,200 sections were made in all.

After the blocks were removed for sectioning the remainder of the specimen was then cleared by a modified Spalteholtz technique and the lymph nodes dissected out under transillumination, sectioned, and their position charted on the original drawing. In tumors lying above the peritoneal reflexion, the mesentery adjacent to the bowel wall which was removed for sectioning was cleared. In tumors below the peritoneal reflexion the perirectal fat was included in the sections.

RESULTS OF STUDY

Of the 126 carcinomas studied, 93 whose lower margin was from 5 to 18 centimeters inclusive above the dentate line were used as the main basis of this report as it is this area of the bowel which is most concerned in the present controversy. In 76 of the 93 tumors the operation in which they were removed was considered curative by the surgeon and in 17 it was considered palliative. Definite retrograde mural spread was found in 18 specimens. It occurred in 9, or over one-half, of the 17 specimens removed by palliative resection and in 9, or 12 per cent, of the 76 curative resections.

The extent of downward spread varied from 1 to 7 centimeters. The maximum spread of 7 centimeters occurred in a specimen from a palliative resection. The greatest extension in a curative resection was 4.0 centimeters. In 67 of the 76 curative resections there was no retrograde spread. In 7 specimens there was downward extension of less than 5 millimeters. As there was some doubt as to whether this represented true distal spread they were not included among these cases.

In this group of 93 tumors, 52 were removed by abdominoperineal resection, 32 by anterior resection with removal of some portion of the inferior mesenteric artery, 4 by simple wedge resection, and 2 by resection with inversion of the bowel distally and colostomy (Hartmann).

In the 5 tumors whose lower margin was less than 5 centimeters above the dentate line, 2

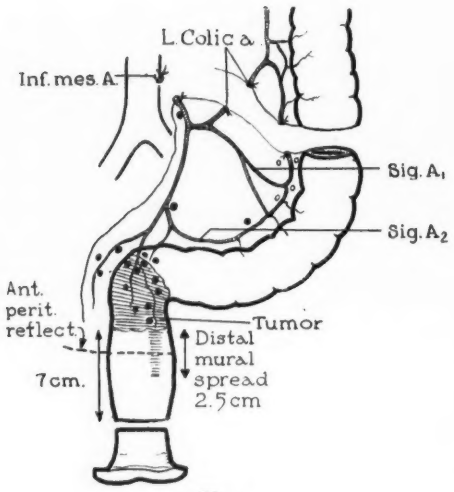

Fig. 4.

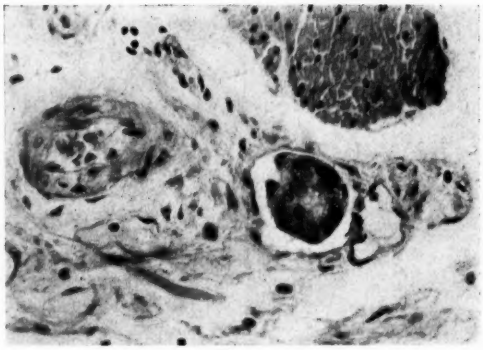

Fig. 5.

Fig. 4. Case 2. A carcinoma of the rectosigmoid removed by palliative abdominoanal pull-through resection with high ligation of the inferior mesenteric artery at the aorta. Metastases were found in 18 of 45 nodes in the cleared specimen. In addition to lateral spread in the paracolic lymphatics of about 8 centimeters, there was distal mural spread of 2.5 centimeters.

Fig. 5. Case 2, Subserosal lymphatic plugged with tumor cells. ×290.

showed retrograde spread for a distance of 2 centimeters. Both were removed at operations considered to be curative.

In the group of 28 tumors lying more than 18 centimeters above the dentate line, 4 showed slight retrograde spread from 1.0 to 1.5 centimeters in extent. All were removed by curative resections. Most were from the mid and lower sigmoid, but 4 were from the descending colon.

The tumor in Case 1 was extremely invasive and unique in several respects. It involved the bowel for a distance of 12 centimeters, from 6.5 to 18.5 centimeters above the dentate line. At operation no evidence of metastasis was found except for enlarged nodes along the inferior mesenteric artery and about the aorta. The surgeon believed that these nodes were presumably involved and the operation was a palliative one; yet he felt optimistic enough to do a high ligation of the inferior mesenteric artery at the aorta along with the abdominoperineal resection. After clearing the specimen 63 out of 67 nodes were found involved including the highest ones at the point of ligation of the artery at the aorta. Paracolic nodes along the marginal vessels of the sigmoid were also involved because of blockage of the main lymphatic route along the inferior mesenteric vessels. This represented a lateral lymphatic spread along the sigmoid colon of about 15 centimeters. Sections taken below the tumor showed retrograde spread distally in the lymphatics to below the dentate line, a distance of 7.0 centimeters. Sections taken through the bowel wall above the tumor also showed the perivascular and perineural lymphatics filled with tumor cells chiefly in the subserosa. Many small veins were also invaded. Sections of the tumor itself showed an extremely anaplastic growth similar to the linitis plastica type seen in the stomach. The patient died of pneumonia 8 days after operation. Autopsy disclosed metastases in the periaortic nodes.

In Case 2 the tumor was similar in many ways. It was also of the linitis plastica type with involvement of 18 out of 45 nodes found on clearing the specimen. There was lateral retrograde spread above the tumor along the paracolic lymphatics and retrograde spread below the tumor for 2.5 centimeters ending in an involved node. Nodes along the inferior mesenteric artery were involved up to the aorta. The resection was considered a palliative one by the surgeon because of multiple tumor implants on the pelvic peritoneum.

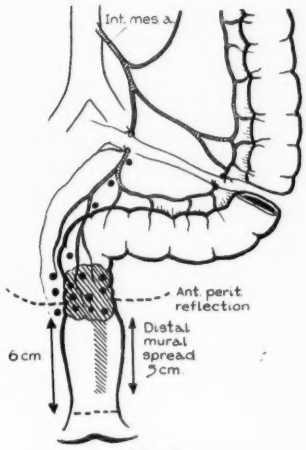

Fig. 6.

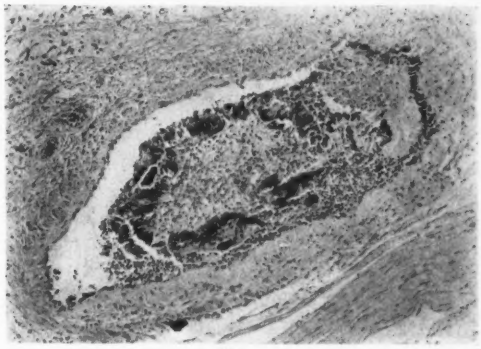

Fig. 7.

Fig. 6. Case 10. A carcinoma of the rectosigmoid removed by palliative abdominoperineal resection. Metastases were present in 19 of 21 nodes found. There was distal mural spread of 5 centimeters in the subserosa and perirectal tissues.

Fig. 7. Case 9. Tumor cells in a subserosal vein 2.5 centimeters below the tumor. ×67.

In Case 10 the tumor was also extremely anaplastic, metastasizing to 19 of 21 nodes found. The most proximal node along the inferior mesenteric artery was involved. A high ligation of the artery was not done as the resection was considered palliative because of tumor implants on the pelvic peritoneum. Three small veins were found invaded by tumor cells in sections of the tumor. Distal spread was seen in the lymphatics just outside the muscularis for 5 centimeters.

In Case 9 the tumor was of interest because it represented the only one in this series in which retrograde spread occurred primarily through the veins which were involved distally in the subserosa for 3.5 centimeters. This type of tumor dissemination has been previously described by Dukes and Bussey. The resection was considered curative by the surgeon. The tumor was grade II and had not metastasized to any lymph glands. The lymphatics below the tumor were not involved.

In Case 12 the tumor was one of the few we have had in which the submucosal lymphatics were the ones chiefly involved. The lesion was a colloid one of the signet ring cell type, grade III, and had metastasized to 14 out of 26 nodes cleared. It was considered curative at operation. The sections showed retrograde spread distally for 4 centimeters.

In Case 13 the tumor was unusual in that it had spread distally by direct extension through the muscularis for 2.8 centimeters. The overlying mucosa was intact. Direct spread of this extent is rare. The lymph nodes, lymphatics, and veins were not involved. The resection was considered a palliative one at operation because of invasion of the prostate and adjacent tissues.

In Case 3 the tumor was of interest as it was the only one showing retrograde spread in the lymphatics in the absence of lymph node metastases. The extent of spread was only 1 centimeter, however, and may not be significant.

In 14 of the 18 tumors with retrograde spread situated 5 to 18 centimeters above the dentate line, the lymphatics were the chief channels of invasion. In the other 4 tumors, one showed distal spread by permeation of a vein and 3 others showed direct extension distally in the muscularis. Lymphatic invasion occurred in all layers of the bowel wall, occasionally in the submucosa, but most often in the subserosa or in its continuation below the peritoneal reflexion as the fatty layer within the fascia propria of the rectum. It usually occurred in the perivascular tissues near an artery or vein. Perineural involvement was less frequent and less extensive.

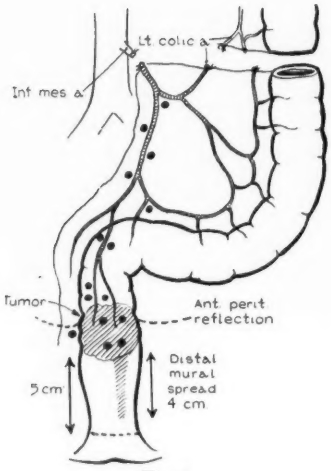

Fig. 8.

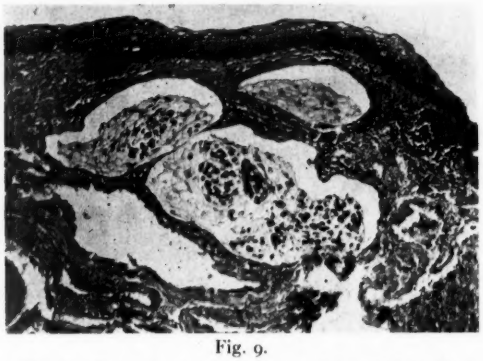

Fig. 9.

Fig. 8. Case 12. A carcinoma of the rectosigmoid removed by curative abdominoperineal resection with high ligation of the inferior mesenteric artery. Metastases were found in 14 of 26 nodes in the cleared specimen. There was distal mural spread of 4 centimeters in the submucosal lymphatics.

Fig. 9. Case 12. Tumor cells of colloid type in the submucosal lymphatics of the anal canal. ×64.

The muscularis showed lymphatic invasion least often. Occasionally, as in Case 13, it was involved by direct spread from the primary tumor without invasion of the other layers.

Retrograde venous invasion was infrequent and was of primary importance in only 1 specimen (Case 9) which has already been mentioned.

As one would expect retrograde spread was usually accompanied by numerous node metastases higher up which were demonstrated by the clearing technique. In only 4 specimens did it occur in the absence of node metastasis. In 1 of these the spread was caused by vein invasion, as already noted, in the second specimen by direct extension in the muscularis, and in the other 2, although the lymphatics were involved, the involvement was for only 1 centimeter distally. In all specimens the distal spread was apparently in continuity whether by the lymphatics or by the veins.

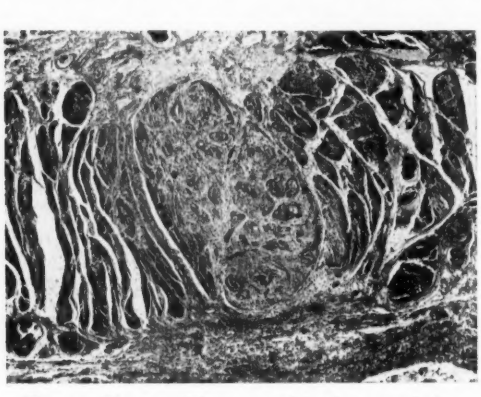

Fig. 10. Case 13. Direct spread in the muscularis 2.5 centimeters below the tumor. ×16.

In the specimens of the 93 tumors lying from 5 to 18 centimeters above the dentate line, no lymph node metastases were found in the cleared tissues below the tumor after the blocks had been removed for sectioning. However, in 8 of the 18 specimens showing distal mural spread, node metastases were seen in the sections of the bowel wall taken from these blocks. This represents an incidence of extramural distal spread to the nodes of 8.6 per cent in the 93 tumors in this group. One lymph node was nearly 4 centimeters below the tumor and another 2.5 centimeters below it. All the others were 1 centimeter or less from it. In the curative cases alone, the incidence of extramural spread to the nodes was 3.9 per cent.

In only 2 of the 18 specimens showing distal spread was an involved node the most distal evidence of tumor extension. In all the others, except for 3 which spread by direct extension

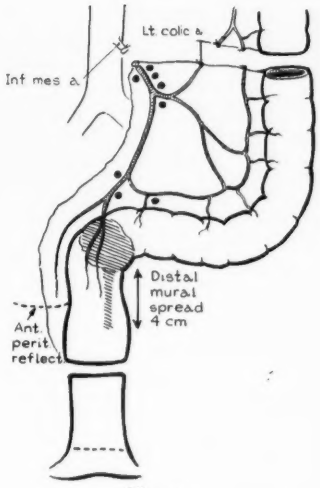

Fig. 11.

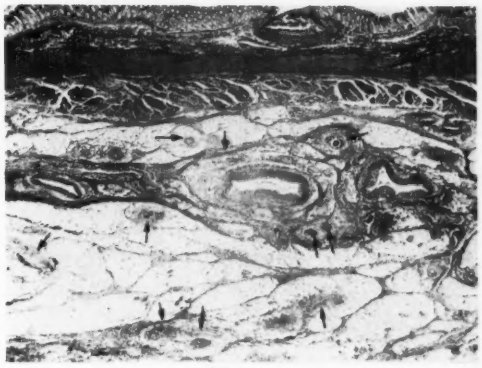

Fig. 12.

Fig. 11. Case 18. A carcinoma of the rectosigmoid removed by curative anterior resection with high ligation of the inferior mesenteric artery. Metastases were found in 8 of 11 nodes in the cleared specimen. There was distal mural spread of 4 centimeters.

Fig. 12. Case 18. Perivascular lymphatics filled with cancer cells 2 centimeters below the tumor.

and the one with invasion of the veins, a lymphatic filled with tumor cells was found at the lowest point of invasion.

COMMENT

On the basis of our results on retrograde extension of tumors lying between 5 to 18 centimeters from the dentate line and found to be curative at operation, a margin of 5 centimeters below the tumor would have been adequate in all. This was also true for the tumors lying both above and below this area. In only 1 patient in the whole series, whose tumor showed distal spread of 7 centimeters would this margin have been inadequate. In this patient the resection was palliative. In the group of 76 patients with tumors between the 5 and 18 centimeter levels and resected with hope of cure, 67 had no retrograde spread. Of course it is possible that some intramural extensions of cancer cells at greater distances below the tumor may have been missed by this method of study and might have been detected if serial sections had been taken. However, we were impressed by the ease with which a permeated lymphatic, once discovered, could be followed to its apparent termination in most cases by successive sections at intervals of 250 to 500 microns.

It became apparent from a study of the histology of the tumors and the gross specimens before and after clearing that those with retrograde spread had many characteristics in common. The tumors were nearly always advanced invasive lesions of high grade malignancy. When compared with tumors which did not have distal spread they showed a far higher incidence of node metastasis and vein invasion and a much higher proportion of tumors microscopically anaplastic and grossly annular in circumference.

The higher incidence of node metastases in specimens with retrograde spread is not surprising, as it is the very presence of these metastases which blocks the normal flow of lymph upward and forces it to take its new course. Node metastases were present in every specimen showing retrograde spread involving the lymphatics except 1 in which the spread was only for 1 centimeter and which may not be significant. In the tumors with node metastases lying from 5 to 18 centimeters above the anal canal the average number of involved nodes per specimen was 12 when retrograde spread was found and only 3 when it was absent.

As tumors removed for palliative reasons, whether with or without distal spread, repre-

TABLE I.—DISTAL INTRAMURAL SPREAD OF TUMORS 5 TO 18 CENTIMETERS INCLUSIVE FROM DENTATE LINE

Case No.	Path. No.	Curative or palliative	Cm. above dentate line	Histologic grade	Dukes type	Nodes sectioned	Node metastases	Vein invasion	Annularity of tumor	Colloid type	Retrograde spread		
											Type of spread	Site	Extent below tumor, cm.
1	A19540	Palliative: aortic lymph node metastasis	6.5	III	C	67	63	+	Annular	o	Lymphatic	All layers, especially subserosa	7.0
2	A19926	Palliative: pelvic peritoneal implants	8.0	III	C	45	18	+	Annular	+	Lymphatic	Subserosa	2.5
3	A20297	Curative	8.0	I	A	21	o	o	¼	o	Lymphatic	Subserosa	1.0
4	A21593	Curative	12.0	II	C	23	1	o	Annular	o	Lymphatic	Subserosa	1.0
5	A22471	Palliative: pelvic peritoneal implants	17.0	III	C	20	2	+	4/5	o	Lymphatic	Subserosa	1.0
6	A22704	Curative	10.0	II	C-2	41	12	o	Annular	o	Direct	Muscularis interna	1.0
7	A23634	Curative	10.0	II	C	19	4	o	4/5	o	Lymphatic	Subserosa	1.0
8	A25531	Palliative: pelvic peritoneal implants	7.0	III	C	30	14	+	Over ½	o	Lymphatic	All, especially submucosa	2.0
9	A26612	Curative	10.0	II	B	28	o	+	Annular	o	Venous	Subserosa	3.5
10	A26626	Palliative: pelvic peritoneal implants	6.0	III	C-2	21	19	+	Annular	+	Lymphatic	Subserosa	5.0
11	A27617	Curative	7.0	II	C	16	4	+	Annular	o	Direct	Muscularis externa	1.0
12	A29724	Curative	5.0	III	C-2	26	14	o	Annular	+	Lymphatic	Submucosa	4.0
13	A29980	Palliative: invasion of prostate	5.0	II	B	19	o	o	Annular	o	Direct	Muscularis externa	2.8
14	A31240	Palliative: invasion of sacrum	12.0	II	C	12	3	o	¼	+	Lymphatic	Subserosa	4.0
15	A32324	Palliative: invasion of lateral pelvis	11.0	II	C	14	9	o	Less than ½	o	Lymphatic	Subserosa	2.0
16	A32414	Palliative: invasion of lateral pelvis	9.0	II	C	45	9	o	Annular	o	Lymphatic	Subserosa	1.0
17	A33215	Curative	6.0	III	C-2	20	9	+	Annular	o	Lymphatic	Subserosa	1.5
18	A36337	Curative	12.0	III	C-2	11	8	+	Annular	o	Lymphatic	All, especially subserosa	4.0

sent a more advanced stage of the disease, it is not surprising that they should prove to be more invasive and malignant as a group than those removed as curative resections.

The incidence of vein invasion as given in Table II was based on a quick survey of the sections of the tumor and was, therefore, lower than it might have been had a more careful study been done.

For purposes of grading, the tumors were divided into 3 grades—I, II, and III—according to whether they were well, moderately, or poorly differentiated. As shown in Tables I and II, the most malignant tumors were usually those that had the greatest distal spread whereas grade I tumors had the least. However, we question whether the grade of the tumor, as determined by a biopsy before operation, should be used as a guide for deciding what is an adequate margin of uninvolved bowel below the tumor in a specific case as Quer, Dahlin, and Mayo seem to suggest. One or two biopsies taken from a tumor show only very limited and superficial portions of it and do not necessarily represent the histology of the tumor as a whole. Moreover the grade of the tumor is only one of a number of factors which may affect the likelihood of retrograde spread. In a large series of cases its influence undoubtedly can be demonstrated but in any

TABLE II.—COMPARISON OF TUMORS WITH AND WITHOUT DISTAL SPREAD REMOVED BY CURATIVE AND PALLIATIVE RESECTION 5 TO 18 CENTIMETERS INCLUSIVE ABOVE DENTATE LINE

	Curative resections						Curative and palliative resections					
	With distal spread (9 tumors)		Without distal spread (67 tumors)		Total (76 tumors)		With distal spread (18 tumors)		Without distal spread (75 tumors)		Total (93 tumors)	
	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent
Lymph node metastasis (all specimens cleared)	7	77.7	32	47.8	39	51.3	15	83.3	40	53.3	55	59.1
Dukes type: A	1	11.1	10	14.9	11	14.4	1	5.5	10	13.3	11	11.8
B	1	11.1	25	37.3	26	34.2	2	11.1	25	33.3	27	29.0
C	7	77.7	32	47.8	39	51.3	15	83.3	40	53.3	55	59.1
Histologic grade: I	1	11.1	24	35.8	25	32.9	1	5.5	25	33.3	26	27.9
II	5	55.5	40	59.7	45	59.2	9	20.0	46	61.3	55	59.1
III	3	33.3	3	4.5	6	7.9	8	44.4	4	5.3	12	12.9
Vein invasion	4	44.4	12	17.9	16	21.1	9	50.0	16	21.3	25	26.8
Complete annularity	7	77.7	15	22.4	22	28.9	12	66.6	20	26.7	32	34.4

particular case it is not a reliable guide to treatment.

Willis, Gray, Westhues, and others have maintained that lymphatic spread from the primary tumor to the regional nodes is by lymphatic emboli. When nodes have become blocked by tumor cells retrograde embolism may occur. It is probably only late in the disease when lymph stasis has occurred, that lymphatic permeation becomes important. In the sections from our specimens the invasion of the lymphatics appeared to be continuous and suggested lymphatic permeation. It has been our impression that the presence of tumor cells in perivascular lymphatics is usually evidence of retrograde permeation and blockage of lymph flow by metastatic nodes higher up.

The poor prognosis in patients with tumors showing retrograde spread is seen in the follow-up results. Only 2 of 9 such patients, with tumors lying from 5 to 18 centimeters above the anal canal and operated on with hope of cure, are alive and apparently well, although followed for less than 2½ years after operation. In both of these patients retrograde spread was minimal. Four of the remaining 7 patients have died of cancer and 3 are alive with persistent disease. These poor results cannot be attributed to retrograde spread per se and an inadequate margin of uninvolved bowel distally, as in only 1 of the 9 patients was an anterior resection performed, and in this patient the margin of bowel below the tumor was 6 centimeters. In all the other patients an abdominoperineal resection was done. Only 2 of the 9 patients with palliative resections in this group are alive and both have definite persistent cancer.

Two of the 4 patients with tumors lying 18 centimeters or more above the dentate line and showing retrograde spread are still well after a short postoperative period and 2 are alive with recurrent disease. All had curative resections. Both patients with tumors less than 5 centimeters above the dentate line and showing retrograde spread had curative resections. One has died of cancer and the other is well 2⅓ years after operation.

The poor prognosis for these patients is not surprising in view of the anaplasia and extensive node metastasis which these tumors show.

SUMMARY AND CONCLUSIONS

1. Retrograde intramural spread from 1 to 7 centimeters in extent was found in 18 out of 93 carcinomas situated from 5 to 18 centimeters above the dentate line. It occurred in 9, or over one-half, of the 17 tumors removed as palliative resections and in 9, or 12 per cent, of 76 tumors removed as curative resections.

2. The maximum distal intramural spread in a curative resection was 4 centimeters in the 93 tumors lying 5 to 18 centimeters above the anus, 2 centimeters in the 5 tumors lying below 5 centimeters, and 1.5 centimeters in

the 28 tumors lying above the 18 centimeter level. In the 5 to 18 centimeter group there were 2 other curative tumors with retrograde spread of 4 centimeters.

3. Retrograde spread was chiefly by way of the lymphatics, usually those of the subserosa and perirectal fat. It appeared to be caused by the blockage of the upward flow of lymph by lymph node metastases and permeation in continuity of the obstructed lymphatics. Occasionally it occurred as the result of permeation of a vein and rarely from direct extension in the muscularis from the tumor itself. The maximum spread by vein was 3.5 centimeters and by direct extension 2.8 centimeters.

4. Retrograde intramural spread is usually found in advanced tumors of high grade malignancy with a much higher incidence of node metastasis, vein invasion, and annular involvement of the bowel than those without distal spread. It occurs most often in tumors so advanced that only a palliative resection can be done. Even in curative resections, the prognosis for the patient is very poor.

5. In curative resections on tumors between 5 to 18 centimeters above the dentate line distal intramural spread did not appear to have great significance. A margin of 5 centimeters of uninvolved bowel would apparently have been adequate in every case. Less than this seems inadvisable and more is preferable. Sixty-seven of 76 patients had no retrograde spread.

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REDUCTION OF INTUSSUSCEPTION BY BARIUM ENEMA

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THE standard operative technique for manual reduction of an intussusception involves increasing the pressure within the intussuscipiens to force the intussusceptum back. In essence, the surgeon, by squeezing the bowel distal to the intussusception, increases the intraluminal pressure and forces the intussusception back, exactly as does the fluid in the hydrostatic pressure method, except that the enema does not contuse the wall of the bowel or abrade the serosa.

The case for hydrostatic pressure reduction of intussusception, whether by saline enema or by barium enema under fluoroscopic control, is to be found in the writings of Hirschsprung (6, 7) and his lineal descendants in Copenhagen, Koch and Oerum, and Monrad, in the writings of Nordentoft, Sjöström, Hellmer, and others in Scandinavia, where the method has always been popular, and in the writings of the Australians, Nelson, and particularly Hipsley (4, 5). It has been pointed out (15) that comparative study of the mortality rates reported by those practicing immediate operation and those attempting primary hydrostatic pressure treatment reveals that the latter group at once showed a lower mortality, and one which has not till recently been matched by clinics resorting to operation primarily. Despite this we do not think that today the argument for or against the use of either method can be based solely on the statistics of mortality rates. Up to the time of this report we have had no deaths in the 65[1] patients treated by hydrostatic pressure reduction. However, in the large clinics resorting to primary operative therapy, as demonstrated by the results of Gross in Boston, Chaffin (19) in Los Angeles, and Benson in Detroit, only those children should now be expected to die who are irretrievably moribund at the time of admission to the hospital. Nevertheless, a series of cases with appreciable mortality rates has been reported by Kahle and associates. We believe that the mode of treatment employed may result in a serious difference in the length of hospital stay, in the incidence of complications, and perhaps even in the number of children moribund on admission.

In clarification of this last statement, the last 5 deaths from intussusception occurring at The Johns Hopkins Hospital (13)—the last in 1946—were all in children in whom there was a serious delay in establishing the diagnosis. We encourage a high index of suspicion and willingly administer barium enemas, as a pedagogic point, whenever the diagnosis of intussusception is suggested, even though we may be convinced it is unlikely in the given instance. The extreme in this respect is represented by Hellmer of Lund, who performed 390 negative barium enema studies during the period 1933 to 1947 in which he treated 162 actual cases of intussusception (with a mortality of 4.9 per cent). However, one need not go to this more than 2 to 1 ratio in order to encourage physicians and pediatricians to send their patients in at the first suspicion of intussusception.

The morbidity rate must continue to favor those patients treated primarily by barium enema, because over 75 per cent of them will have escaped an anesthetic and an incision with whatever incidence of complications is taken to attend these. By the same token the duration of hospital stay will be shorter in the group in which only 25 per cent or fewer have had an operation. One factor which has always affected mortality and morbidity in intussusception is the necessity for intestinal resection. As Hellmer points out and our experience supports, resections are appreciably more often performed in clinics where immediate operation is the rule. Manual reduction of

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[1]Sixty-two of these patients were treated at The Johns Hopkins Hospital, Baltimore, Maryland, and the last 3 at The Mount Sinai Hospital, New York.

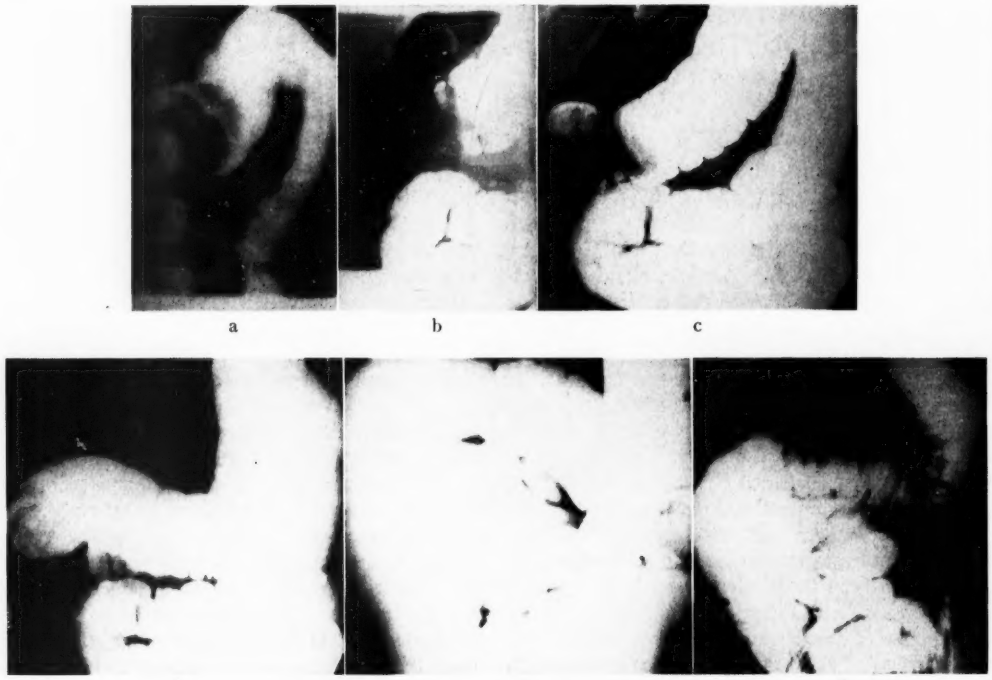

Fig. 1. A 3¾ year old female with an intussusception of 17 hours' duration. She had had abdominal pain and vomiting during this time and had passed no blood. She was prostrated, listless, markedly dehydrated with eyes sunken. Her breath was sweet and her urine contained 3+ acetone. Her temperature was 38 degrees centigrade with white blood cell count of 17,000. There was an easily palpable, transverse, sausage-shaped mass in the epigastrium. While intravenous fluids were being administered and after the operating room had been notified, the catheter was inserted in the rectum and barium administered. The intussusception was met and seen in (a), the transverse colon to the left of the midline, and in the course of 15 minutes it reduced steadily and evenly well into the ileum without any prolonged delay at any point. Charcoal was administered into the stomach through a gastric tube. Six hours after reduction, the child passed stool with a good deal of flatus and some barium. Twelve hours after reduction, an enema showed the charcoal which had been given immediately after reduction. She ran a low grade fever for 4 days, was afebrile on the fifth and was discharged.

Note the sharp meniscoid edge of the advancing barium column. When the colon is over distended (e) it may obscure the filling of small bowel although in this instance several loops of what were apparently small bowel filled readily in areas remote from the cecum. The post evacuation film (f) shows many filled loops of small bowel framed by the partially empty colon.

an intussusception may be difficult and trying. It is to be feared that resection is not rarely demanded by the pathologic changes induced by the manipulative reduction rather than by the intussusception itself. Furthermore, it happens that viable bowel is resected because it has been mistaken as damaged beyond recuperation. Hydrostatic pressure reduction is infinitely less traumatic to the bowel than manual reduction at open operation. As evidence of this is the appreciable incidence in many reports of subsequent mechanical intestinal obstruction from adhesions, occurring after open reduction of intussusception but not after enema reduction.

The great mass of clinical experience acquired over the past 70 years in the treatment of intussusception, both by operation and by reduction by hydrostatic pressure, has demonstrated what seems to us adequately by pragmatic test the safety and superiority of primary reduction by hydrostatic pressure (17). Two of the objections still raised to the method are that gangrenous bowel may be reduced and that the bowel may perforate under pressure during reduction. A series of experi-

ments was undertaken to determine the likelihood of such mishaps and to study the pathologic changes and the clinical course in animals. Intussusceptions were produced in dogs at open laparotomy with sterile precautions (14). After intervals of 18, 28, 38, and 48 hours the dogs were anesthetized and the abdomen was reopened under sterile conditions. The serosal surface of the neck of the intussusception was cultured and under direct observation an attempt was made to reduce the intussusception by a saline enema under 3 feet of pressure.

In no instance was gangrenous bowel reduced. In no instance was there a perforation of the bowel. Whenever an intussusception could be reduced by hydrostatic pressure, the animals survived indefinitely. In no instance did an animal with a reduced intussusception have peritonitis, abscess, fistula, or any other complication to suggest that nonviable bowel might have been reduced. In no instance did bowel, reducible or irreducible, rupture. Of special interest were the cultures from the serosa of the intussusceptions. Numerous pathogenic organisms were recovered and sometimes several from 1 animal. Pathogenic organisms were frequently found on the surface of perfectly viable bowel, whose reduction was compatible with survival.

It is our feeling at present, that the treatment of choice for intussusception in infants and children is radiologically controlled hydrostatic pressure reduction followed by operation if necessary to confirm reduction or complete the reduction if the lesion persists. It has been our policy to attempt hydrostatic pressure reduction in all children regardless of the duration of the intussusception. A study (16) of the case histories of a large group of children, correlating mortality with duration of the disease before the beginning of treatment, indicates that there is almost no mortality in the first 24 hours of the disease and a rapidly increasing mortality up to 72 hours and then a sharp decrease in mortality. This is obviously due to the fact that children surviving more than 72 hours with intussusception before treatment has begun will often have a nonstrangulating type of intussusception. The clinical and experimental evidence would indicate that with the method to be described, there is little or no danger of reducing bowel which is gangrenous, little or no danger of rupture of the bowel, that the force of the hydrostatic pressure in irreducible intussusceptions is expended on the healthy bowel of the intussuscipiens.

In our hands, as soon as the diagnosis of intussusception is made or suspected, the operating room is advised to prepare for operation. The infant is taken to the fluoroscopic room and a Foley bag catheter with a 45 cubic centimeter balloon is inserted into the rectum and the balloon distended. It is essential that the catheter be ungreased, so that it may be less readily expelled, and that the buttocks be firmly strapped together with adhesive tape. It is surprising how large a balloon can be expelled by even a small infant. If the child is in shock or dehydrated, blood or intravenous fluids are administered. In most cases the stomach is aspirated to avoid the danger of vomiting in the dark-room. The reservoir, filled with an ordinary suspension of barium, is elevated to 3 feet above the table and the barium permitted to run into the bowel under fluoroscopic observation. A large reservoir, quite full, will obviate delays during the treatment. The barium will usually be seen to run rapidly into the rectum and colon until the head of the barium column meets the point of the intussusception. At this point, the rounded head of the advancing barium column suddenly becomes concave, forming a meniscus around the point of the intussusception, much as would a column of barium in the vagina outlining the cervix. As pressure increases, the meniscus lengthens, the horns extending until suddenly the intussusception is pushed back and the meniscus flattens out again. This process is repeated, sometimes with extreme rapidity, until the intussusception is reduced to the cecum and through the ileocecal valve. One should take care that the barium flows freely into the ileum. In 1 instance it was possible to observe that the barium passed 3 or 4 inches up into the ileum and then stopped while the characteristic meniscus was still discernible. This child was taken at once to the operating room and found to have an intussusception in the ileum about 6 inches

above the ileocecal valve, the reduction of which was readily completed.

At times, the entire reduction proceeds swiftly and smoothly and at others the reduction hangs at one point or another until the intussusception suddenly gives way. It is most important to maintain uninterrupted hydrostatic pressure with smoothly flowing barium. As long as the reduction proceeds, however stubbornly and slowly, the treatment should be persisted in. Failure is more often due to unexpected expulsion of the barium than to any other cause. If the child should expel the barium around the tube, the entire process is repeated with greater care to avoid leakage. Traction on the catheter will at times be required to produce a tight seal. Thus far we have never failed to reduce the intussusception at least to the cecum. Delays of 10 to 15 minutes may occur at several points, most often at the cecum. Intussusceptions have been completely reduced, even when the intussusception had presented outside the anus and when it had to be replaced into the rectum to permit the introduction of the catheter. It is important to be satisfied that the barium has gone through the ileocecal valve well into the ileum and that the intussusception has been completely reduced. Under no circumstances is the abdomen manipulated in any way. If the distended cecum and sigmoid overlap, obscuring the field so that it is difficult to see the ileum, it may be useful to turn the child upon the abdomen, letting the child's own weight displace the bowel and separate the obscuring loops.

Immediately after the completion of the reduction, powdered charcoal is deposited in the patient's stomach through a tube and 6 hours later an enema is administered to recover the charcoal and prove beyond doubt the completeness of the reduction. The successful reduction of an intussusception is indicated by the following criteria: (1) the free entrance of barium well into the small bowel, (2) return of the barium together with feces or flatus, (3) disappearance of the mass, (4) clinical improvement of the child who often falls into a natural sleep, and (5) subsequent recovery in the stool of charcoal given by mouth, or the appearance of a blood free stool.

Since 1939 we have treated 65 patients for intussusception with barium enema as the primary treatment. There have been no deaths in the entire series. In 50 of the cases, 77 per cent, the intussusception was reduced by barium enema alone. In the remaining 15 cases, operative completion of the reduction was required, usually through a McBurney incision. If there is any doubt about the completeness of reduction, there is little harm in exploration of the ileocecal junction through a small McBurney incision, at which time an appendectomy may be performed. With increasing experience with the method, the percentage of successful reductions by barium enema alone will rise steadily. In our last 21 cases, 19 (90 per cent) were reduced without operation.

A number of objections are regularly raised to the barium hydrostatic pressure treatment: (1) As with any closed method of treatment of acute abdominal conditions, one may be in error as to the diagnosis. However, the diagnosis of intussusception by barium enema is precise and certain. Furthermore, pediatricians who are aware that the presumptive diagnosis of intussusception will lead to an immediate laparotomy may tend to delay the consultation with a surgeon whereas if the presumptive diagnosis of intussusception means no more than a barium enema, surgeons can expect to be called sooner and see their cases at a more favorable time at the cost of performing an occasional barium enema in children with other conditions. (2) Hydrostatic pressure will not reduce ileocecal intussusceptions which are not in the colon. However, in such cases, barium enema will fail to show any intussusception and the children will then obviously have to be explored for the presenting acute abdominal condition which has not been relieved. (3) Hydrostatic pressure will rupture the bowel or will reduce gangrenous bowel. The accumulated experimental and clinical evidence disproves this. (4) In children whose intussusceptions are caused by specific lesions such as polyps or Meckel's diverticula, these lesions will not be disclosed by barium enema. It is fortunate that none of these lesions are such as in themselves to cause serious concern. Thus, 2 per

cent of individuals ordinarily have Meckel's diverticula. Polyps in the small bowel are important only because they cause intussusception and do not usually give rise to carcinomas. If a child has repeated intussusceptions, the intussusception should be reduced by barium enema, careful radiologic studies should subsequently be made and then elective operation should be performed to see whether a specific predisposing cause exists. Such predisposing causes are least common in infants, the group in whom most intussusceptions occur.

Hydrostatic pressure reduction of an intussusception by barium enema is as much a surgical procedure as is the closed reduction of a fracture. It should be performed in a hospital, with fluids or blood being administered and the operating room in readiness. We feel strongly that while the co-operation of a pediatrician and radiologist is helpful and important, hydrostatic pressure reduction should be undertaken by the surgeon whose responsibility it is to decide whether an open operation is to be performed.

SUMMARY

Hydrostatic pressure reduction of intussusception by barium enema has been the method of primary treatment in 65 cases of intussusception in infants and children. In 50 cases (77 per cent) no further treatment was required. In 15 cases a small persistence of the intussusception at the ileocecal valve or cecum was reduced operatively. There were no deaths. In the last 21 cases, 19 (90 per cent) were reduced by barium enema alone.

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DIFFUSE PERITONITIS SECONDARY TO INTESTINAL PERFORATION COMPLICATING MALIGNANT LESIONS OF THE COLON

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THE clinical evidences of malignant tumors of the colon may be considered to be the result of the diverse complications to which these lesions are subject. Obstruction, ulceration, slow perforation with abscess or fistula formation, and intussusception are among the more commonly encountered complications which may indicate the presence of a neoplasm. Generalized peritonitis secondary to perforation of the bowel, although infrequently described as a complication of carcinoma of the colon, is the most lethal of all. Twenty-one cases of generalized peritonitis resulting from perforation of the colon secondary to carcinoma have been collected from the files of the Metropolitan and Flower and Fifth Avenue Hospitals during a 12 year period. It is apparent that the subject deserves greater emphasis than it has received heretofore. The present study was instituted to determine whether diagnostic criteria could be established together with a rational plan of management of this grave sequela of carcinoma of the colon.

INCIDENCE

During the years 1940 to 1952 inclusive, 709 patients with a diagnosis of carcinoma of the colon were registered at the Metropolitan and Flower and Fifth Avenue Hospitals. Of this number, there were 21 cases of generalized peritonitis secondary to acute perforation of the colon resulting from carcinoma, an incidence of 3 per cent.

The perforation occurred at the site of the carcinoma in 18 cases (85.7 per cent); in 3 cases (14.3 per cent), it was situated in a segment of distended but otherwise normal bowel proximal to the obstructing malignant tumor.

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CLINICAL FINDINGS

Symptoms. There were 12 men and 9 women in the group studied. The average age was 67.8 years, the youngest patient being 40 years of age and the oldest, 83.

A majority of the patients (52.4 per cent) had experienced loss of approximately 30 pounds of weight during the year prior to the onset of the present illness. Ten of the patients (47.6 per cent) complained of pain for nearly a year. In every instance except 1 the pain was located in the abdomen; in the exception its location was lumbar. Ten of the patients (47.6 per cent) stated that there had been alterations of bowel habits for a period of about 6 months. Progressive constipation was present in 7 instances, while episodic diarrhea was present in 3. Eight patients (38.1 per cent) had noted gross blood in their stools.

Severe pain was the initial complaint of the present illness in 20 cases (95.2 per cent), in 19 of which it was located in the abdomen. In 1 instance, the initial complaint was severe pain situated in the right shoulder. In only 1 instance was pain absent as a presenting symptom; in this case, the patient, a bedridden arteriosclerotic, suddenly went into shock during the course of a diagnostic work-up.

Abdominal pain was diffuse in 7 instances and localized to the right lower quadrant in 6 cases. Three patients complained of pain in both lower quadrants while, in the remaining 3 cases, it was located in the epigastrium, the left upper quadrant, and the left lower quadrant, respectively. The pain was severe in all cases, constant in 16, and

colicky in 3. In general, the average patient experienced crampy abdominal pain for 3 or 4 days, followed by a sudden, severe, constant pain for about 24 hours prior to admission.

Nine patients (42.9 per cent) did not have a bowel movement for an average of 4 days prior to admission. In 1 instance, there had been complete obstruction for 9 days. One patient had watery diarrhea for 14 hours preceding admission.

Profuse vomiting was a major complaint in 11 instances (52.8 per cent). In 9 cases, the vomitus consisted of gastric or biliary secretions, and in only 2 instances was it described as feculent.

Three patients (14.3 per cent) experienced shaking chills after the onset of the present illness.

In 5 cases (23.8 per cent), the acute episode occurred while the patient was in the hospital undergoing work-up or treatment.

Signs. On admission, the temperature was elevated (average: 101.6) in 14 individuals (66.7 per cent). The pulse rate was above 100 in 11 instances (52.8 per cent). Eleven patients exhibited clinical evidence of shock; 3 of these patients were comatose on admission.

Moderate or marked abdominal distention was noted in 12 cases (57.1 per cent).

The most conspicuous physical sign was the presence of extreme abdominal tenderness, which was observed in all patients. Ten patients experienced generalized abdominal tenderness; in 6 of these individuals, the perforation was situated in the left colon, and in 4, in the right colon. In 7 patients, the tenderness was located principally in the right lower quadrant; in 4 of these cases, the perforation was situated in the right colon, and in 3, in the left colon. Four patients experienced marked tenderness in the left lower quadrant; in each instance, the perforation was situated in the left colon. Thus, with the possible exception of left lower quadrant tenderness, the location of the abdominal tenderness offers no clue to the site of the colonic perforation.

When noted, peristaltic sounds were absent on auscultation in only 5 instances (23.8 per cent). In 2 other cases, peristalsis was diminished.

In 9 patients (42.9 per cent), a palpable mass was observed: by abdominal examination (5 cases) and rectal examination (4 cases).

Laboratory data. The admission hemoglobin level was less than 10 grams in only 2 patients; in both, the value was 9.5 grams. The average leucocyte count was 13,600, with an average of 82 per cent polymorphonuclear leucocytes.

Roentgenographic data. The presence of subdiaphragmatic air was demonstrated in 6 of the 9 patients examined roentgenographically. Examination of the colon by barium enema was performed in 6 cases and demonstrated the presence of a neoplasm in 5. The patient in whom the lesion was not observed by roentgenogram was found to have a carcinoma of the cecum at operation. In 4 of the 6 cases, the barium enema had been performed within 4 days of the acute episode and, for this reason, may have been a factor in precipitating perforation.

Diagnosis. A diagnosis was recorded preoperatively or premortem in 20 cases. The correct diagnosis of generalized peritonitis and perforated bowel associated with intestinal cancer was made in 9 cases (45 per cent). The most common erroneous diagnosis, recorded in 6 instances, was uncomplicated intestinal obstruction secondary to cancer of the large bowel. In 2 patients, the mistaken preoperative diagnosis was acute appendicitis.

Mortality. Sixteen patients (76.2 per cent) were treated surgically with 13 deaths, an operative mortality of 81.25 per cent. Diagnosis was established in the 5 nonsurgical cases by postmortem examination. The surgical procedures employed in the 3 patients who recovered were obstructive-exteriorization resection for a perforated carcinoma of the rectosigmoid in 2 instances, and obstructive-exteriorization resection once for reticulum cell sarcoma of the ascending colon. Other operative procedures employed were cecostomy or proximal colostomy. The absolute mortality rate was 85.7 per cent, i.e. 18 deaths in 21 cases.

PATHOLOGIC FEATURES

There was generalized peritonitis in all cases. In 7 (77.8 per cent) of the 9 cases in which cultures of the peritoneal fluid were made, growth of the following organisms was reported: Staphylococcus aureus in 3 cases, Bacillus coli in 2, Bacillus subtilis in 2, Streptococcus hemolyticus in 1, and alpha streptococcus in 1.

One patient, from whom the peritoneal fluid was not cultured, developed a subcutaneous emphysema of the entire body. The clinical course was highly suggestive of a gas bacillus sepsis.

Diastatic or obstructive perforation of the cecum occurred in 3 cases (14.3 per cent). The primary obstructive neoplasm was situated in the sigmoid in 2 instances, and in the hepatic flexure in the third. Perforation occurred at the site of the tumor in the remaining 18 individuals. In 1 of these cases, there was an intussusception of the terminal ileum, cecum and cecal tumor, and ascending colon into the transverse colon to the splenic flexure with free perforation through the cecal tumor and intussuscipiens.

In 10 instances, an estimation of the size of the perforation was recorded. The average diameter of the perforations was 1.75 centimeters, the smallest being 0.5 centimeter, and the largest 5 centimeters.

In 71.4 per cent of cases, the tumor was situated in the left half of the colon, and in 28.6 per cent, in the right half. The lesion was located in the sigmoid colon in 57 per cent of cases.

A gross description of the perforated tumor was recorded in 17 cases (76.5 per cent), the estimated average size being 6 centimeters. Twelve of the 17 neoplasms (70.6 per cent) involved the entire circumference of the bowel, constricting its lumen. Two were "fungating," and another "plaque-like."

Microscopic data were available in 17 cases and 15 (88.2 per cent) were diagnosed adenocarcinoma. One was a lymphosarcoma of the cecum, and another a reticulum cell sarcoma involving terminal ileum and cecum. Metastatic involvement of the regional lymph nodes was noted in 6 cases (35.3 per cent). There were metastases to the liver in 4, metastases to the spleen in 2, to the lung in 1, and to the spine and ribs in 1.

DISCUSSION

In the presence of carcinoma of the colon, acute perforation may occur either at the site of the malignant lesion or through a segment of distended intestine proximal to the obstructing tumor. The latter condition, termed by Heschl as "diastatic perforation," has received emphasis during the past 2 decades. A "closed loop" is produced by an obstructing lesion distally and a competent ileocecal valve proximally. The progressive accumulation of gas and fluid produces a high pressure gradient which causes bursting of the colon at its most vulnerable area above the obstruction—usually, the cecum. The ileocecal valve, however, is incompetent in at least 50 to 60 per cent of individuals, a factor which may explain the infrequent occurrence of obstructive perforation of the cecum. Ravid, in his collective review of diastatic perforations, was able to report upon only 81 cases in the world's literature from 1831 to 1949. More recently, Rack reported a 1.5 per cent incidence of diastatic perforation of the cecum in 509 patients with carcinoma of the colon admitted to the Cleveland City Hospital. In Dennis' series of 35 cases of acute colon obstruction secondary to carcinoma, there was only 1 case of cecal perforation. On the other hand, 19 cases of acute perforation *at the site of* a carcinoma of the colon have been reported in the Anglo-American literature during the past 12 years. It is possible that even this is not a true picture of the incidence either because of failure to recognize the condition, or simply because the complication is thought to be due to delay or even neglect, and not worthy of report. In our compilation not only did free perforations through the carcinoma of the colon occur with uniform annual frequency, but they were 6 times as common as diastatic perforations. These findings have led us to believe that any reasonable therapeutic approach should take into consideration the greater potentiality of colonic neoplasms to perforate locally rather than to perforate at a distance.

Malignant lesions of the colon which are subject to intraperitoneal perforation tend to conform to a rather constant gross pattern. The lesions are bulky and often palpable clinically. They are usually associated with a high degree of intestinal obstruction by virtue of their circumferential growth around the wall of the bowel. Perforation tends to occur through an area of necrosis which has developed as a result of ischemia. This state of local circulatory embarrassment may be based upon the following factors: (1) the large tumor may "grow away" from its blood supply; (2) the high intraluminal pressure resulting from complete intestinal obstruction may compress the intramural vessels supplying the carcinomatous area; and (3) intravascular thrombosis of the small vessels may develop and progress as a result of transluminal migration of bacteria through the diseased bowel wall.

Study of our group of patients suggests that those presenting this formidable complication of bowel cancer present a rather well defined and uniform clinical syndrome, particularly when the lesion is located in the left colon. The patient, who is frequently older than the average patient with carcinoma of the colon, complains of considerable weight loss, episodes of crampy abdominal pain, and increasing constipation for about 6 months. Three or 4 days prior to admission the symptoms have progressed rapidly; bouts of crampy pain are more frequent and more intense. With increasing obstipation, distension develops; episodes of vomiting are frequent. Twenty-four to 48 hours prior to admission, the character of the pain changes, becoming markedly severe and constantly present. Most patients exhibit signs of shock. When the abdomen is examined, marked distention and extreme abdominal tenderness, both direct and rebound are noted. A mass is often detected by abdominal or rectal palpation. Pneumoperitoneum may be demonstrated by the diminution of liver dullness to percussion or else by means of roentgenographic examination of the abdomen.

The mortality rate resulting from operative treatment of this emergency was 81.25 per cent in our series, and 78.9 per cent in 19 surgical cases reported in the recent literature. These facts suggest a need for critical analysis of past methods of management. As a result of the present study, the following principles of surgical treatment are proposed. Since perforation through the site of the lesion appears to be more common than diastatic perforation and the location of abdominal tenderness is not generally indicative of the site of the rupture, the abdomen should be entered preferably through a left rectus incision. The neoplasm is situated in the left colon in the majority of cases. If perforation has occurred through a lesion in a readily mobilized segment of the bowel, the neoplasm should be resected by an obstructive resection procedure. In our opinion, primary anastomosis is not indicated because of the presence of markedly dilated thin-walled bowel with local circulatory embarrassment in a critically ill, aged patient with generalized peritonitis. In addition, immediate effective decompression is difficult to obtain. The increased time necessary for execution of a primary resection and anastomosis is a factor contraindicating its employment. When mobilization cannot be accomplished readily, a loop sigmoid or transverse colostomy should be constructed above the lesion, and drains inserted to the site of perforation. All grossly contaminating particles should be removed. Also, the lumen of the colonic segment between the colostomy and the site of perforation should be cleansed as thoroughly as possible to prevent further contamination. Cecostomy or Witzel types of enterostomy are not satisfactory as definitive measures, since they fail to divert completely the fecal stream, nor are they reliable means of decompression in the presence of "closed loop" obstructions. However, cecostomy may be indicated occasionally in association with obstructive resection of the left colon when immediate decompression of a tremendously dilated proximal loop is considered imperative. In the event that a diastatic perforation of the cecum or ascending colon is found, a separate right midrectus incision should be made. The cecal perforation should be plicated, reinforced with omentum, a transverse colostomy performed, and drains placed to the site of the perforation.

In the rare instance of perforation through a carcinoma of the right colon, the procedure of choice in a good risk patient without marked distention is right hemicolectomy with primary anastomosis of ileum to transverse colon.[1] When this is not feasible, obstructive resection with exteriorization of ileum and transverse colon, after the method of Lahey, is recommended.

SUMMARY

A study of 21 cases of free perforation associated with carcinoma of the colon has been presented. In this series, perforation at the site of the neoplasm was 6 times as frequent as diastatic perforation. The most prominent clinical features were obstipation, severe and constant abdominal pain, distention of the abdomen with extreme abdominal tenderness, and frequently the presence of a mass detected by abdominal or rectal examination. The majority of the perforations occurred through large adenocarcinomas which completely obstructed the bowel. Only 18.75 per cent of the patients survived emergency surgical treatment. A definitive plan of surgical management is proposed, emphasizing the desirability of immediate resection of the perforated neoplasm.

[1]Since completion of this study, right hemicolectomy with primary anastomosis has been performed successfully in a 38 year old man with free perforation of a reticulum cell sarcoma of the cecum and diffuse peritonitis.

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CARDIOVASCULAR EVALUATION IN SURGERY

I. Operative Risk in Cancer Patients with Bundle Branch Block

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SURGICAL therapy for various cancers may be restricted by the condition of the patient prior to and during surgical intervention. The cardiovascular status plays a major role in this appraisal and ofttimes is the limiting factor for adequate operative attack.

There are many excellent reviews on the subject concerning the evaluation of patients with heart disease as a surgical risk. This communication does not consider the general problem of surgical risk of cardiac patients but concentrates on the preoperative appraisal of patients with the electrocardiographic diagnosis of bundle branch block.

In the age group in which cancer is most often detected, heart disease may coexist. The presence of any preoperative electrocardiographic abnormality, particularly bundle branch block, should alert the surgeon as to the increased risk introduced by the basic cardiac disorder. Since bundle branch block may frequently indicate a serious underlying cardiac disease, an accurate evaluation of cardiac status prior to contemplated surgery is imperative.

METHODS AND MATERIALS

Electrocardiograms (standard, unipolar, and 6 precordial leads) were taken routinely on all patients admitted to the urologic division of the Francis Delafield Hospital. When the electrocardiogram was diagnosed as abnormal, further cardiac evaluation was requested prior to surgical procedures. In order to extend the series of cases with bundle branch block, patients with similar electrocardiographic findings on the surgical division were considered as well. The diagnosis of the various types of bundle branch block was made according to standard acceptable criteria.

The urologic and surgical services were charged with the evaluation of the primary focus of the neoplasm, the extent of the disease, and the possible benefits which might accrue from surgical interference. The cardiac division collaborated in the general supportive preparation of the patient for such surgery.

After the diagnosis of any cardiac disease, and of bundle branch block in particular, was made, adequate cardiac preparation was advised and thence supervised. Further suggestions were made as to choice of anesthesia and in regard to any special precautions during the surgical procedure. Whenever necessary, the cardiologist assisted in the direct management of the case in the operating room. This cardiologic care was continued postoperatively, whenever needed.

The data under discussion are based on studies of 20 males and 1 female from the urologic division (Table I) and of 26 males and 9 females from the surgical division (Table II).

The majority of patients were in advanced stages of cancer. Many of the surgical procedures, however extensive, were merely palliative.

RESULTS

Composition of the series. In the 21 urologic patients the electrocardiogram revealed right bundle branch block in 14 men and 1 woman, incomplete or Wilson type of bundle branch block in 2 other men, and left bundle branch block in 4 additional men. Nine out of 14 men with right bundle branch block had arteriosclerosis as the etiologic factor, while in 5 men the etiologic factor was hypertensive cardiovascular disease. The cause of the woman's

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TABLE I.—AGE DISTRIBUTION, SEX DISTRIBUTION, AND ETIOLOGIC CLASSIFICATION OF 21 CASES OF VARIOUS TYPES OF BUNDLE BRANCH BLOCKS FOUND ON UROLOGIC SERVICE

Age, Years	R.B.B.B.		L.B.B.B.		R.B.B.B. (Wilson)		Total	
	M.	F.	M.	F.	M.	F.	Male	Female
51–55	2*	0	0	0	0	0	2	0
56–60	2*	0	1*	0	1‡	0	4	0
61–65	1*	0	0	0	0	0	1	0
66–70	3* 2†	0	1† 2*	0	0	0	8	0
71–75	1* 3†	0	0	0	0	0	4	0
76–80	0	1*	0	0	1*	0	1	1
Total	14	1	4	0	2	0	20	1

*Atherosclerotic heart disease
†Hypertensive cardiovascular disease
‡Posterior myocardial infarction

right bundle branch block was arteriosclerotic heart disease. In 3 of the 4 men with left bundle branch block and in the 2 men with right bundle branch block (Wilson) arteriosclerosis was considered the etiologic factor.

The cases from the surgical service included 13 men with right bundle branch block of whom 5 were arteriosclerotic (Table II), and 3 of whom had hypertensive cardiovascular disease. Secondary carcinoma of the bundle of His, hypertensive cardiovascular disease combined with arteriosclerotic heart disease and chronic cor pulmonale secondary to metastatic heart disease, arteriosclerosis combined with anterior myocardial infarction and with hypertensive cardiovascular disease each accounted for 1 case. Four women had right bundle branch block, 3 of which were caused by arteriosclerosis and the fourth by hypertensive cardiovascular disease.

Four men and 2 women had left bundle branch block. In 3 of the men and in 1 of the women arteriosclerosis was the etiologic factor; in the remaining man and woman, hypertensive cardiovascular disease was causally related to the left bundle branch block.

Six men and 1 woman had right bundle branch block (Wilson type). Arteriosclerosis was the etiologic factor for 2 of the men and for the woman. In 2 of the men, chronic cor pulmonale was the contributing cause; in 1 man it was hypertensive cardiovascular disease; and in the remaining man arteriosclerosis and hypertensive cardiovascular disease were the etiologic causes.

Three men and 2 women had indeterminate bundle branch block. Arteriosclerosis, rheumatic heart disease, and hypertensive cardiovascular disease were the etiologic factors in the men, while rheumatic heart disease and arteriosclerosis were the etiologic agents in the women.

Surgical procedures. Tables III and IV list the operation, cardiac diagnosis, anesthetic agent, and duration of the various operative procedures[1] in both the urologic and surgical groups. There were 66 operative procedures (18 major and 48 minor) in the 21 patients comprising the urologic group and 92 operative procedures (33 major and 59 minor) in the 35 patients comprising the surgical group. Delineation of operative procedures into "major" and "minor" categories was arbitrary in the present analysis. The body site and extent of surgery, the duration of anesthesia, the condition and the age of the patient together determined the classification. In addition, the correlation between multiple procedures and postoperative recuperation contributes to the evaluation of the surgical risk.

Complications. On the urologic service there were 4 men and 1 woman who experienced complications following surgery. Four of the patients, 3 men and 1 woman, had right bundle branch block on an atherosclerotic basis. One man had right bundle branch block on a hypertensive basis. The anesthetic agent or duration of anesthesia was not causally related to the complication.

[1]Unfortunately no discrimination was made on the anesthetic records between the time the agent was first given and either duration of anesthesia in the operating room or the time the patient reacted postoperatively. This accounts for the wide time variations in performance of identical procedures by the same surgeon and the seemingly inordinate duration of many minor procedures listed in Tables III and IV. For example Case 1 of the urology group was recorded as having anesthesia for 2¼ hours. Cystoscopy and open perineal prostatic biopsy ordinarily require 15 minutes each. Even with transfer of the patient from one operating room to another and allowing 15 to 20 minutes for frozen section microscopy of the biopsy, the duration of anesthesia would appear unreasonably long. For present purposes this form of error serves only to emphasize the value of adequate cardiac management of the patient. Fundamentally, the relationship of prolonged anesthesia to favorable surgical outcome of the cardiac patient rather than to lack of surgical speed is most relevant.

On the surgical service there were 11 complications (7 men and 4 women). Five men had right bundle branch block (3 on a hypertensive basis, 2 on chronic cor pulmonale) while 1 man each had left bundle branch block and Wilson type bundle branch block on an arteriosclerotic basis. Two women had right bundle branch block (1 on an arteriosclerotic and 1 on hypertensive cardiovascular disease) whereas the other 2 women had left bundle branch block (both caused by hypertensive cardiovascular disease). Nine patients, 5 men and 4 women, went into shock postoperatively; 1 man experienced paralytic ileus and a small wound abscess within 24 hours after surgery.

All complications (mainly shock and hypotension) responded to simple, routine therapy. One patient (S-22) had experienced cardiac decompensation following common bile duct exploration at another hospital 6 months prior to admission and operation here. Despite this history, cardiac preparation with digoxin permitted a 3¾ hour cholecystectomy and jejunostomy at this hospital during which only hemorrhagic shock occurred caused by an acute blood loss of 600 cubic centimeters during surgery, which was corrected rapidly and adequately by blood transfusion at the time.

On the urologic service only 1 man (U-11) required cardiac preparation prior to surgery in the form of digitoxin and sodium restriction for 48 hours preoperatively. This patient suffered clinically and laboratory diagnosed "hypoadrenal syndrome." It appears most unlikely that 48 hours of sodium privation, particularly in the presence of normal serum sodium preoperatively, could so rapidly induce hypoadrenalism. Cortisone and intravenous infusion of saline corrected the syndrome within 3 days.

There were 4 cases (3 men and 1 woman) on the surgical service who required cardiac preparation for surgery. In 7 of the 11 patients who developed complications no preoperative cardiac preparation had been deemed necessary. The basis for offering or withholding preoperative cardiac medication will be elucidated in the discussion which is presented in the following.

TABLE II.—AGE DISTRIBUTION, SEX DISTRIBUTION, AND ETIOLOGIC CLASSIFICATION OF 35 CASES OF VARIOUS TYPES OF BUNDLE BRANCH BLOCK FOUND ON SURGICAL SERVICE

Age, years	R.B.B.B.		L.B.B.B.		R.B.B.B. (Wilson)		Indeterminate		Total	
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
31–35	0	0	0	0	1‖	0	0	0	1	0
46–50	1*	0	1*	0	0	0	0	0	2	0
51–55	0	0	1*	0	0	0	0	0	1	0
56–60	0	0	0	1†	0	0	1*	1♯	1	2
61–65	1*	1†	0	0	1* 1†	0	0	0	3	1
66–70	3† 1§	1*	0	0	1‖	0	0	0	5	1
71–75	1♯ 2* 1*‡	0	1* 1†	0	1*	1*	1♯ 1†	1*	9	2
76–80	1* 1*†	1*	0	0	0	0	0	0	2	1
81–85	1†	1*	0	1*	1*†	0	0	0	2	2
Total	13	4	4	2	6	1	3	2	26	9

*Atherosclerotic heart disease
†Hypertensive cardiovascular disease
‡Anterior myocardial infarction
§Carcinoma of bundle of His
‖Cor pulmonale (chronic)
♯Rheumatic heart disease

It is noteworthy that there were no deaths in the 56 consecutive patients comprising this study.

Of all the complications encountered none was unique to bundle branch block. These postoperative difficulties commonly occur following surgery for benign lesions and often in young, vigorous patients.

Table V summarizes the types of complications, the treatment, and the outcome of the complications on both services.

DISCUSSION

Risk of surgery has in recent years decreased remarkably through improved surgical techniques and judicious management of fluid balance, antibiotics, pressor agents, and general medical support. These factors now permit extensive elective surgery in aged individuals even in the presence of cardiovascular disorders. One of the frequently encountered cardiac disorders which requires careful evaluation and control is bundle branch block.

TABLE III.—CARDIAC DIAGNOSES AND OPERATIVE PROCEDURES FOR UROLOGIC PATIENTS

Case No. Hospital No.	Operative procedure	Date	Bundle branch block	Anesthesia					Duration, hrs.—min.
				Local	Spinal	General induction stage*			
						1	2	3	
U1 523	1. Cystoscopy 2. Open perineal prostatic biopsy	3-15-51 3-21-51	Left	Yes		Pentothal	N_2O-O_2		2′15″
U2 697	Cystoscopy; bronchoscopy	7-3-51	Right	Yes					
U3 787	1. Biopsy, abdominal wall 2. Prefrontal lobotomy	8-22-51 8-24-51	Left	Yes		Pentothal	N_2O-O_2		3′
U4 268	1. Transurethral biopsy bladder tumor 2. Suprapubic cystotomy; radium implant bladder tumor; unilateral ovariectomy 3. Transurethral biopsy bladder	11-7-51 11-20-51 1-16-52	Right		Nupercaine 5 mgm.	 Ether-O_2 Pentothal	 Cyclopropane-O_2 N_2O-O_2		1′30″ 2′30″ 1′
U5 244	Cystoscopy	11-29-51	Left	Yes					
U6 358	1. Cystoscopy 2. Transurethral prostatic resection; radical perineal prostatectomy; bilateral orchiectomy	1-2-52 1-16-52	Wilson	Yes	Nupercaine 5 mgm.	Pentothal	N_2O-O_2		3′30″
U7 1501	1. Cystoscopy 2. Transurethral prostatic biopsy and resection; open perineal prostatic biopsy; radical perineal prostatectomy; bilateral orchiectomy	3-14-52 3-18-52	Right	Yes	Nupercaine 5 mgm.	Pentothal	N_2O-O_2		3′45″
U8 1600	Cystoscopy; transurethral biopsy bladder tumor; transurethral prostatic resection	4-29-52	Right		Nupercaine 5 mgm.				1′40″
U9 1593	1. Transurethral biopsy bladder 2. Translumbar aortogram 3. Nephrectomy, right 4. Open perineal prostatic biopsy; perineal prostatic enucleation, conservative	4-29-52 5-10-52 5-20-52 6-12-52	Left	 Yes	Nupercaine 5 mgm.	 Pentothal Pentothal Pentothal	 N_2O-O_2		1′15″ 15″ 1′35″ 1′55″
U10 1604	1. Cystoscopy 2. Open perineal prostatic biopsy	5-5-52 5-8-52	Wilson	Yes	Nupercaine 5 mgm.				1′25″
U11 1866	1. Cystoscopy 2. Open perineal prostatic biopsy 3. Bilateral orchiectomy 4. Bone marrow aspirations	9-29-52 10-7-52 10-16-52 11-6-52 & 11-21-52	Right	Yes Yes Yes Yes	Nupercaine 5 mgm.			O_2	1′15″
U12 2579	Cystoscopy; open perineal prostatic biopsy	1-9-53	Right		Nupercaine 5 mgm.			O_2	2′
U13 2744	1. Transurethral bladder biopsy 2. Transurethral prostatic biopsy 3. Transurethral prostatic resection 4. Cystoscopy 5. Open perineal prostatic biopsy 6. Open perineal prostatic biopsy; transurethral prostatic resection	3-9-53 3-27-53 4-7-53 5-19-53 5-21-53 9-8-53	Right	 Yes 	Nupercaine 5 mgm. Nupercaine 5 mgm. Nupercaine 5 mgm. Nupercaine 5 mgm., adrenalin chloride Pontocaine 10 mgm.				1′30″ 1′15″ 2′30″ 2′15″ 1′30″
U14 2756	1. Cystoscopy; open perineal prostatic biopsy 2. Lumbar sympathectomy	3-20-53 5-4-53	Right		Nupercaine 5 mgm. Nupercaine 5 mgm.				1′5″ 2′
U15 2855	1. Cystoscopy 2. Open perineal prostatic biopsy	5-4-53 5-5-53	Right		Nupercaine 5 mgm.				1′15″
U16 2966	1. Cystoscopy; bilateral ureteral catheterization; open perineal prostatic biopsy 2. Radical perineal prostatectomy 3. Bilateral orchiectomy	6-25-53 6-30-53 7-16-53	Right	Yes Yes	Nupercaine 5 mgm.	 Ether-O_2	 Surital	 Cyclopropane-O_2	2′ 3′
U17 3043	1. Cystoscopy 2. Open perineal prostatic biopsy 3. Cystoscopy	8-12-53 8-13-53 9-23-53	Right	Yes Yes	Nupercaine 5 mgm.				1′

TABLE III.—CARDIAC DIAGNOSES AND OPERATIVE PROCEDURES FOR UROLOGIC PATIENTS —CONTINUED

Case No. Hospital No.	Operative procedure	Date	Bundle branch block	Anesthesia					Duration, hrs.—min.
				Local	Spinal	General induction stage*			
						1	2	3	
U18 3023	1. Transurethral biopsy bladder tumor	9-18-53	Right		Nupercaine 5 mgm.				2′30″
	2. Transurethral bladder biopsy	9-25-53			Nupercaine 5 mgm.				1′45″
U19 3752	1. Cystoscopy	10-1-53	Right	Yes					
	2. Open perineal prostatic biopsy	10-7-53			Nupercaine 5 mgm.				1′45″
	3. Biopsy rib marrow	10-20-53		Yes					
	4. Transurethral prostatic resection	10-20-53			Nupercaine 5 mgm.	N_2O-O_2	Pentothal		2′30″
U20 3909	Cystoscopy; open perineal prostatic biopsy; bilateral orchiectomy	12-10-53	Right			N_2O-O_2	Surital		2′30″
U21 4068	1. Cystoscopy; open perineal prostatic biopsy; bilateral orchiectomy	2-4-54	Right		Nupercaine 5 mgm.				3′40″
	2. Transurethral prostatic resection	2-11-54			Pontocaine 10 mgm.				2′30″
	3. Transurethral prostatic resection	2-29-54			Nupercaine 5 mgm.				2′30″

*No systemic difficulties encountered during anesthetic induction in any of these 21 cases.

Bundle branch block is identified as a depression in conduction in the region of the bundle of His and in the left and right bundle branches. The condition is diagnosed decisively by the electrocardiogram which reveals a *P-R* interval of greater than 0.12 second and *QRS* complex of more than 0.11 second in duration. The diagnosis of left or right bundle branch block is delineated by use of precordial leads. However, this technique is not infallible and one must resort occasionally to the use of the term "uncertain type" bundle branch block. It is generally held that right bundle branch block offers a slightly better prognosis than left bundle branch block although it is the less common type.

Bundle branch block occurs most frequently in males past the age of 50 years. The etiologic factors, in order of importance, are coronary arteriosclerosis, hypertensive cardiovascular disease, scarring from rheumatic myocarditis, and rheumatic heart disease. Finally, infectious and destructive processes, such as lues or tumor, may injure the bundle of His or the bundle branches. Congenital bundle branch block is extremely rare.

One must contend with the practical consideration, in assessing for surgery a patient suffering from bundle branch block, of deciding whether the cardiac condition or the malignant lesion is the determining factor of life expectancy. In evaluating the bundle branch block, several factors must be taken into account. First, the type of block is important. Right bundle branch block, as stated, usually offers a better prognosis than left, i.e., survival of 3 to 4 years and 2 to 3 years, respectively, following the discovery of the condition. The best survival records are seen in patients with S type or indeterminate bundle branch block. Second, the underlying etiology for the bundle branch block is significant. The presence of coronary atherosclerosis offers a more serious prognosis than congenital bundle branch block. On the other hand, the existence of cardiovascular disease with bundle branch block probably indicates more severe cardiac disease than does a past history of diphtheria, which is thought to be causally related to bundle branch block. Third, abnormal cardiac function resulting directly or indirectly from the bundle branch block bears upon medical evaluation of the problem. The presence of congestive heart failure, angina pectoris, and cardiac enlargement concomitant with bundle branch block usually indicates a worse prognosis.

Questions may arise as to the criteria and procedure of the preoperative medication which one is to employ in the individual case. Basically, any patient is considered a candidate for preoperative medication when one or more of the following cardiac abnormalities are found: (1) congestive cardiac failure of any

TABLE IV.—CARDIAC DIAGNOSES AND OPERATIVE PROCEDURES FOR SURGICAL PATIENTS

Case No. Hospital No.	Operative procedure	Date	Bundle branch block	Anesthesia					Duration, hrs.—min.
				Local	Spinal	General induction stage			
						1	2	3	
1 23	Transurethral prostatic resection	2-2-51	Right			Pentothal	N_2O-O_2		1′15″
2 530	1. Cystoscopy 2. Open perineal prostatic biopsy; radical perineal prostatectomy; bilateral orchiectomy	3-8-51 3-14-51	Indeterminate		Nupercaine 5 mgm. ↓				3′30″
3 6	Herniorrhaphy, umbilical	4-10-51	Indeterminate			Ether-O_2	Cyclopropane-O_2		1′45″
4 666	1. Cystoscopy 2. Cystoscopy; bilateral ureteral catheterization 3. Sigmoidectomy; partial colectomy; cecostomy	6-2-51 6-22-51 6-28-51	Right			Pentothal Ether-O_2	Cyclopropane-O_2		4′45″
5 111	1. Cholecystectomy 2. Hysterectomy, vaginal	6-28-51 7-20-51	Indeterminate			Ether-O_2 Ether-O_2	Cyclopropane-O_2 Cyclopropane-O_2		1′45″ 2′10″
6 256	1. Biopsy, supraorbital ridge 2. Dental extraction, multiple 3. Aspiration biopsy, bone marrow 4. Excision basal cell tumor, face; dermatome graft	11-5-51 11-20-51 4-12-52 6-9-52	Left	Yes Yes 		Pentothal Pentothal	N_2O-O_2 N_2O-O_2		1′15″ 1′45″
7 271	1. Thoracentesis 2. Thoracentesis 3. Thoracentesis	11-7-51 11-8-51 12-7-51	Wilson	Yes Yes Yes					
8 999	1. Laparotomy, exploratory; colostomy 2. Liver biopsy	2-14-52 4-3-52	Left	 Yes		Cyclopropane-O_2*	Pentothal		2′15″
9 2901	1. Rectosigmoid resection 2. Cystoscopy	4-4-52 11-9-53	Indeterminate	Yes	Pontocaine 15 mgm.				3′30″
10 1068	Radium implantation, cervix	4-8-52	Wilson	Yes					
11 1579	1. Cystoscopy; bladder biopsy 2. Cystoscopy, bilateral ureteral catheterization; transurethral biopsy bladder lesion 3. Incision and drainage abdominal wall abscess 4. Incision and drainage abdominal wall abscess	4-22-52 4-24-52 5-12-52 6-10-52	Wilson	 Yes 	Nupercaine 5 mgm. Nupercaine 5 mgm.	 Ether-O_2	 Pentothal Cyclopropane-O_2	 N_2O-O_2	1′50″ 2′45″ 1′55″
12 1101	1. Esophagoscopy 2. Gastroscopy 3. Thoracotomy; esophagogastrectomy; splenectomy 4. Esophagoscopy 5. Esophagojejunostomy	4-23-52 4-30-52 5-8-52 8-18-52 8-19-52	Left	Yes Yes Yes ↓ 	 	 Ether-O_2 Ether-O_2	Surital N_2O-O_2 N_2O-O_2	 	45″ 7′50″ 8′20″
13 498	Aspiration biopsy bone marrow	8-19-52	Right	Yes					
14 1450	Colostomy	10-30-52	Wilson	Yes	Intercostal xylocaine				1′40″
15 2000	1. Biopsy left leg 2. Midthigh amputation, left	12-14-52 6-8-53	Wilson	Yes	Pontocaine 10 mgm.				2′15″
16 2087	Biopsy breast nodule and skin lesion	12-19-52	Left	Yes					
17 2118	1. Thoracentesis 2. Bronchoscopy	1-15-53 1-26-53	Right	Yes Yes					
18 2120	1. Proctoscopic biopsy 2. Cystoscopy 3. Abdominoperineal resection 4. Transurethral prostatic resection 5. Ileal resection	1-16-53 1-21-53 1-23-53 4-30-53 10-9-53	Wilson	Yes Yes 	 Nupercaine 5 mgm. 	 Ether-O_2 Cyclopropane-O_2	 Cyclopropane-O_2 Succinyl choline	 Surital and tubocurare	5′30″ 1′40″ 3′30″

↓ S
*T

TABLE IV.—CARDIAC DIAGNOSES AND OPERATIVE PROCEDURES FOR SURGICAL PATIENTS —CONTINUED

Case No. Hospital No.	Operative procedure	Date	Bundle branch block	Anesthesia					Duration, hrs.—min.
				Local	Spinal	General induction stage			
						1	2	3	
19 2524	Biopsy groin ulcer	2-17-53	Right	Yes					
20 2248	1. Biopsy facial ulceration; skin graft	3-5-53	Right	Yes					15″
	2. Biopsy axillary mass	3-9-53		Yes					
	3. Biopsy ear	3-17-53				Pentothal	N_2O-O_2		
	4. Excision parotid tumor	3-30-53				N_2O-O_2	Cyclopropane-O_2	Demerol	4′50″
	5. Eyelid pedicle graft	4-17-53		Yes					
	6. Tracheostomy	11-6-53		Yes		Pentothal	N_2O-O_2	Procaine	45″
	7. Section N. V, IX, X (upper vagus)	11-13-53				N_2O-O_2	N_2O-O_2		7′15″
21 2222	1. Bronchoscopy	3-12-53	Right	Yes					
	2. Biopsy internal mammary nodes	4-5-53				Demerol	N_2O-O_2	Seconal and procaine	1′25″
	3. Bronchoscopy	4-6-53		Yes					
	4. Aspiration biopsy bone marrow	4-9-53		Yes					
	5. Biopsy left leg	6-26-53		Yes					
22 2985	1. Duodenostomy	5-5-53	Right		Nupercaine 15 mgm.				6′
	2. Biopsy liver; cholecystectomy; jejunostomy	8-13-53				Ether-O_2	N_2O-O_2	Pentothal	3′45″
23 2891	1. Proctoscopic biopsy	5-12-53	Right		Nupercaine 5 mgm.				
	2. Excision rectal polyp	5-19-53			Nupercaine 5 mgm.				1′
24 2432	Subtotal gastrectomy	6-12-53	Right			Ether-O_2	N_2O-O_2	Procaine	2′45″
25 3889	1. Subtotal gastrectomy	6-15-53	Right			Ether-O_2	Ether-O_2		2′10″
	2. Esophagoscopy; laparotomy, exploratory	1-14-54				N_2O-O_2	Surital		4′30″
26 2489	1. Bronchoscopy	6-17-53	Right	Yes					
	2. Lobectomy, left lower	7-21-53				Ether-O_2	N_2O-O_2		3′45″
27 3613	Laryngoscopy	8-3-53	Right	Yes					
28 3629	1. Bronchoscopy	8-10-53	Left	Yes					
	2. Thoracotomy	8-14-53				Ether-O_2	Cyclopropane-O_2	N_2O-O_2	3′
29 3057	1. Tracheostomy	8-22-53	Indeterminate	Yes					
	2. Radium implantation, cervix	10-21-53							
	3. Thoracentesis	11-2-53		Yes					
30 3050	1. Biopsy, tonsil	9-3-53	Right	Yes					
	2. Gastrostomy	10-27-53		Yes					2′
31 3687	1. Pneumonectomy	10-1-53	Left			Cyclopropane-O_2	Ether-O_2	Surital	4′
	2. Thoracotomy; incision and drainage lung abscess	10-26-53				Pontocaine	Surital		2′15″
	3. Thoracoplasty	1-25-54				Cyclopropane-O_2	Ether-O_2	Surital and succinyl choline	3′15″
32 3729	Biopsy abdominal wall mass	10-5-53	Wilson	Yes					
33 3762	1. Excision nasal ala; skin graft	10-9-53	Right	Yes					1′30″
	2. Biopsy facial ulceration; skin graft	10-26-53		Yes					
34 3802	1. Aspiration biopsy bone marrow	10-26-53	Right	Yes					
	2. Biopsy supraclavicular node	10-28-53		Yes					
	3. Angiogram	11-5-53		Yes					
35 3785	1. Excision skin nodule	10-26-53	Right	Yes					
	2. Aspiration biopsy bone marrow	12-5-53		Yes					

↓ Supplemental pentothal administered
*Transient hypotension in this patient

TABLE V.—CORRELATION OF POSTOPERATIVE COMPLICATIONS WITH CARDIAC DISEASE, ANESTHESIA, AND TREATMENT OF COMPLICATIONS

Patient No.	No. of operations	Cardiac etiology	R.B.B.B.—age		L.B.B.B.—age		Wilson R.B.B.B.—age		Duration of anesthesia, hrs.—min.	Local or general anesthesia	Complication	Treatment
			Male	Female	Male	Female	Male	Female				
U4	3	A.S.H.D.		76↓					1′	General	Hypotension	Shock position
U6	1	A.S.H.D.	76↓						—	Local	Pulmonary embolism	Anticoagulants
U16	2	A.S.H.D.	61↓						3′	General	Shock	Transfusion
U11	3	H.C.V.D.	70*						—	Local	Hypoadrenal syndrome	Cortisone and saline
U20	1	A.S.H.D.	75↓						2′30″	General	Shock	Shock position
							Surgical Service					
4	3	A.S.H.D., H.C.V.D.	76*						4′45″	General	Paralytic ileus and small wound abscess	Intubation; I & D
8	1	A.S.H.D., H.C.V.D.			72↓				2′05″	General	Shock	Shock position
12	3	H.C.V.D.				60↓			7′50″	General	Shock	Transfusion
12	5	H.C.V.D.				60↓			8′20″	General	Shock	Transfusion
20	7	A.S.H.D., angina	73↓						7′15″	General	Shock	Transfusion
22	2	H.C.V.D.	81*						3′45″	General	Shock	Transfusion
24	1	A.S.H.D.		78*					2′45″	General	Shock	Transfusion
26	2	Cor pulmonale	71*						3′45″	General	Shock	Transfusion
25	2	H.C.V.D.		62↓					4′30″	General	Shock	Transfusion
18	5	Cor pulmonale					69↓		3′30″	General	Shock	Shock position
22	1	H.C.V.D.	81↓						Operation was at another hospital		Heart failure	Treated at another hospital

H.C.V.D. Hypertensive cardiovascular disease
A.S.H.D. Arteriosclerotic heart disease
*Required cardiac medication prior to surgery
↓ Did not require cardiac medication prior to surgery

type or degree; (2) cardiac enlargement or dilatation shown by x-ray examination; and (3) electrocardiographic abnormalities indicating "strain patterns" of hypertensive cardiovascular disease, auricular fibrillation, or ventricular ectopic rhythms. Patients with any of these findings are usually digitalized by means of digitoxin or digoxin. The former is chosen when a protracted need of a digitalis preparation is anticipated. Usually a total of 1.2 milligrams is given in divided doses at least 48 hours prior to operation. Maintenance doses are usually 0.1 to 0.2 milligram daily. Digoxin is a digitalis preparation which is rapidly excreted making maintenance difficult. This property, however, is exploited in preparing the patient for surgery in as much as it involves far less danger of prolonged digitalis toxicity in hypokalemia. Eighty per cent of administered digoxin will be excreted within 24 hours, whereas at least 14 days are required for excretion of a like percentage of digitoxin.

Other cardiac supportive measures are also adopted. Sodium restriction for at least 48 hours prior to operation is instituted in all those patients who do not have frank congestive failure to offset hypernatremia and edema which could result from infusion postoperatively. The hemoglobin is usually brought up to 10.0 grams prior to surgery. Blood loss is estimated carefully during the operative procedure.[1] Both fluid replacement and hemoglobin are maintained at optimal levels because it is well known that anoxia and shock

[1]Preoperative and postoperative assessment of plasma volume may be made by a modification of the T-1824 colorimetric determination described by Plentl and Gelfand. They defined total blood volume as 75 to 80 cubic centimeters per kilogram body weight and erythrocyte mass as 30 to 35 cubic centimeters per kilogram.

are much more serious in circulatory disorders than in most other types of concomitant systemic disease.

Quinidine sulfate or quinidine gluconate is used freely and prophylactically (0.2 gm. 3 times a day after meals and at bed time) on all patients who (a) are not sensitive to the preparation, (b) undergo thoracotomies, and (c) have aberrant ventricular arrhythmias. Quinidine is usually given in maintenance doses 24 hours prior to operation and continued for at least 5 to 7 days postoperatively. The rationale for giving quinidine to all patients undergoing thoracotomy is to prevent occurrence of cardiac arrhythmias to which these patients are so prone.

During all these surgical procedures, it was emphasized that the oxygen supply be maintained as close to 20 per cent as possible. At no time was the patient permitted to become anoxic.

A word should be said concerning the preoperative medication and type and duration of anesthetic agent. Cardiac patients in particular should be anesthetized quickly to obviate any struggling. One cannot specify the best agent, for this choice rests primarily with the anesthetist. Preoperative medication is encouraged but drugs which are respiratory depressants are to be avoided.

In this series of cases, in which the principles defined for cardiac premedication were scrupulously observed, there was not a single fatality in either urologic or surgical groups. No postoperative complication was serious and they could have easily developed in a younger age group, in noncancerous individuals, or in any patient without known cardiac disease. The completely successful conduction through surgery of all the patients in this series attests to the value of combining the efforts of the cardiologist and surgeon during all phases of the surgical management of the cancer patient.

In no instance was emergency cardiac therapy required during the operative procedure itself, despite the fact that patients with bundle branch block could have experienced exacerbations of their underlying cardiac disorder at any time, expecially during a stress situation such as a surgical procedure.

In general, the incidence of arrhythmia found with bundle branch block is no greater than in patients without cardiac disease. It must be cautioned, however, that in the presence of bundle branch block, ectopic foci in the ventricles may easily predispose to fatal ventricular fibrillation. Auricular arrhythmias in conjunction with bundle branch block are not in themselves serious unless they produce coronary insufficiency or cardiac failure. If an arrhythmia develops during surgery (*proved by electrocardiography*) prompt intravenous digitalization with 2.5 milligrams of digoxin is indicated. If the arrhythmia is ventricular in origin, digitalis is contraindicated, and pronestyl or quinidine may be given intravenously. It must be emphasized that pronestyl may produce severe hypotension which may eventuate in death. Accordingly, noradrenaline is given simultaneously with pronestyl in order to maintain blood pressure. Quinidine should not be given intravenously for the emergency control of cardiac arrhythmia during surgery unless one is thoroughly familiar with the risks involved. Lyons refers to quinidine as a "dangerous drug" in that it predisposes to cardiac arrest. This fear is probably overemphasized; a useful drug such as quinidine should not be withheld when indicated.

From the present study, no correlation could be made between the type of bundle branch block and outcome of surgery. All types of bundle branch block present no greater risk than the underlying etiologic cardiac disease coupled with the degree of cardiac compensation (as evidenced by cardiac enlargement and congestive heart failure).

By way of comparing the present results with those of other investigators, LaDue and associates (3) observed a 5.2 per cent operative mortality in 58 patients who had evidence of healed myocardial infarction. They compared this with a mortality rate of 3.2 per cent in 260 noncardiac patients, also in the seventh decade, who had undergone similar major surgical procedures. There were 24.1 per cent cardiorespiratory complications postoperatively in their group of patients with cardiac disease. Of the patients given cardiac medication prior to surgery, 33 per cent developed cardiorespiratory complications in contrast to only

20 per cent of 40 such patients not given digitalis. In another group of patients reported by dePeyster, Paul, and Gilchrist there were 15 postoperative deaths among 41 patients who had healed myocardial infarction and angina pectoris. Morrison recorded an over-all mortality rate for prostatectomy at New York Hospital of 4.5 per cent in 752 cases. In 90 patients with arteriosclerotic heart disease subjected to prostatectomy in the same hospital, the mortality rate was 20 per cent. Butler, Feeney, and Levine reported an operative mortality rate of 7.7 per cent in 35 surgical patients who had angina pectoris and 44.5 per cent mortality in 20 different cases of healed myocardial infarction.

Morrison found in a group of 65 patients with arteriosclerotic heart disease (including 12 with left bundle branch block, 21 with right ventricular block, and 13 with intraventricular block), a postoperative mortality rate of 8 per cent.

LaDue and his associate (6) also observed a 3.3 per cent mortality in a different series consisting of 58 cases of bundle branch block, which compares favorably with the minimal surgical mortality for any large series of major operative procedures. Their report also emphasizes the relative safety of surgery in patients with bundle branch block.

SUMMARY

1. Twenty-one patients from a urologic service and 35 from a surgical service, all having cancer, were studied as surgical risks on the basis of electrocardiographic diagnosis of bundle branch block. The average age was 66.3 years and 68.1 years for the urologic and surgical services, respectively.

2. Each patient was subjected to one or more major or minor surgical procedures which varied in duration from 1 hour to 8⅓ hours. By an arbitrary classification, 51 major and 107 minor operations were performed on the 46 elderly males and 10 females included in this series.

3. No fatalities occurred in this series.

4. In 4 men and 1 woman, preoperative cardiac preparation was given. Special emergency therapy during surgery was not required in any case.

5. Postoperative complications of relatively minor consequence were encountered in 11 men and 5 women. Shock and hypotension were the most common; these were easily corrected by appropriate therapy. No complication was unique either as to cardiac disease or the existence of cancer.

6. Indications for cardiac preparation were: (a) congestive heart failure, (b) enlarged heart by x-ray examination, (c) history of congestive heart failure in the past, and (d) cardiac arrhythmias which compromised cardiac action. Complete co-operation between the surgeons and the cardiologist was emphasized in the over-all management of the patient.

7. It appears that the judicious use of digitalis and other cardiac drugs, of general or spinal anesthesia, of proper electrolyte and fluid regulation and adequate blood replacement are sufficient to permit extensive radical surgery in elderly, cancerous patients with safety.

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VENOUS OCCLUSION OF LOWER EXTREMITIES IN PARAPLEGIC PATIENTS

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MANY factors known to be predisposing for venous occlusion of lower extremities are present in patients with spinal cord injuries. For this reason, a study was made of 99 patients with cord injury in which phlebography was used in order to demonstrate the site of occlusion. Fourteen patients had either actual, or a history of, unilateral or bilateral swelling of the lower extremities while the remaining majority of 85 was examined at random.

MATERIAL AND METHOD

Of the 99 patients here presented, 67 had clinically complete cord or cauda lesions (physiologic transection) and 32 had clinically incomplete (partial) lesions. Of the complete lesions, 2 were cervical, 60 thoracic, and 5 lumbar; of the incomplete lesions, 7 were cervical, 13 thoracic, and 12 lumbar. Diodrast was used as a contrast medium. The tourniquet technique was used as modified by one of us (T.B.M.). The procedure was carried out (C.A.C.) as follows: 30 cubic centimeters of a 35 per cent solution of diodrast were injected in a superficial vein of the dorsum of each foot within 1 minute. Two tourniquets were in place at the midthighs and ankles of each respective leg, and immediately 3 x-ray exposures were made of each lower leg, thigh, and pelvis respectively. Thus it was possible to study the deep intercommunicating and collateral venous system.

Table I shows the incidence of venous occlusions which was present in 58 cases or 58.6 per cent. It was equally high in complete and incomplete lesions although the distribution according to the level of the lesion differs in that a venous block was rarely seen with complete cervical or lumbar lesions. Patients with complete thoracic lesions had the highest incidence of venous blocks. In contradistinction, venous blocks were almost equally distributed among patients with incomplete lesions. Only 41 or 41.4 per cent of the 99 patients showed normal phlebograms.

Table II shows the incidence of venous occlusion with spastic or flaccid paralysis, respectively. Venous block was much more frequent (5 to 1) in patients with complete and flaccid lesions than in those with complete, spastic lesions. In patients with incomplete lesions this ratio was smaller (not quite 2 to 1). The distribution of blocks was rather equal in the incomplete group. Complete thoracic lesions were found more frequently accompanied by a block. The ratio of spasticity to flaccidity was 16 to 25 among the patients without venous occlusion. Eight patients with spasticity and 20 with flaccidity had complete lesions. Venous occlusions were present in 29 (45 per cent) of all spastic and in 70 (64 per cent) of all flaccid patients.

Evaluation of the incidence of venous occlusion in correlation to the duration of the cord lesion showed: The highest rate was observed during the first year (a total of 19 patients of which 8 were 6 months or less after injury), another peak (23 patients) was seen during the third and fourth year. During the second year and after 4 or more years, the incidence was 5 and 11, respectively. In comparison the number without venous block was 18 patients during the first year, 9 in the second, 8 in the third and fourth years, and 6 after 4 years and more.

The incidence of venous occlusion in correlation to age was highest in the group between 20 and 30 years of age (29 patients) and somewhat lower in the group between 30 and 40

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TABLE I.—INCIDENCE OF VENOUS OCCLUSION IN 99 PATIENTS

Type of lesion	Block		Normal		Total No.
	No.	Per cent	No.	Per cent	
Complete C	1	1.5	1	1.5	2
T	36	53.6	24	35.8	60
L	2	3	3	4.5	5
Total	39	58	28	42	67
Incomplete C	5	15.6	2	6.2	7
T	8	25	5	15.6	13
L	6	18.7	6	18.7	12
Total	19	59	13	41	32

C, cervical; T, thoracic; L, lumbar

years (21 patients). The decline in the higher age group (40 to 50 years, 3 patients; 50 to 60 years, 5 patients) parallels the lower number of patients. This age distribution was not dissimilar among the patients without phlebothrombosis (20 to 30 years, 28; 30 to 40 years, 8; 40 to 50 years, 2; 50 to 60 years, 3).

Evaluation of the incidence of venous occlusion in relation to laterality, i.e., the right or left extremities, topography, i.e., veins of the pelvis, thigh, and lower leg, and to the level and extent of the cord lesion disclosed no conspicuous relationship between side and the level or extent of the myelopathy. The local distribution of venous occlusion was in the order of frequency: thigh, lower leg, pelvis (41, 34, and 8 instances, respectively). The left side was, though not significantly, more often involved than the right (44 left, 39 right).

Swelling of the lower extremities was observed in 14 instances. It was bilateral in 7 cases (thigh 2, ankles 5), but venous occlusion was present in only 4 patients, of which 2 had bilateral and 2 unilateral venous blocks. It was unilateral in 7 cases; in 1 of these no venous occlusion was found, in another the venous block was contralateral to the swelling, in 4 cases block and swelling coincided ipsilaterally, and in the remaining case a bilateral occlusion existed with a unilateral swelling. Summing up, swelling of the lower extremities was present in 14 patients but only 10 had phlebographic evidence of venous occlusion.

DISCUSSION

In 1949 Cook and Lyons reported the absence of thromboembolic phenomena in 45 paraplegic and tetraplegic patients. However, they used no phlebograms to prove their statement but relied upon clinical and laboratory findings. Our study would then demonstrate that a positive phlebogram is necessary in order to present convincing evidence.

We do not propose to decide whether our patients suffered from thrombophlebitis or phlebothrombosis since this differentiation is still controversial and may be applied to the pathogenesis rather than to clinical manifestation. Three main causes lead to venous occlusion, namely, vein injury, blood changes, and hemodynamic changes. Quite a few conditions are present in paraplegics which cause such changes. Unnoticed injury to the vein by malposition may well invite biochemical, endothelial changes leading to thrombosis. Hypoproteinemia, disturbances of the albumin-globulin ratio, anemia, chronic infection from decubitus ulcers or urinary tract, spinal cord trauma per se, disturbances of calcium metabolism, endocrinologic dysfunction, decreased carbon dioxide combining power, shock, prolonged bedrest, muscular paralysis and atrophy, and pain—briefly severe physical and mental stress—form an arsenal of known predisposing factors.

The incidence of venous occlusion in paraplegics is more than 10 times higher (58.6 per cent) than that reported postoperatively (5 per cent) by Allen, Barker, and Hines. The importance of flaccidity versus spasticity underscores the significance of complete immobilization and muscular atrophy by an over-all ratio of 64 per cent venous blocks in all flaccid as against 45 per cent in all spastic cases. This ratio increases and becomes 5 to 1 when only the group of patients with complete lesions and venous occlusion is considered. Flaccidity following poliomyelitis was considered by Dock to be the cause of thrombosis. Why the distribution differed between patients with complete and with incomplete lesions is not quite clear unless one wants to presume that the incomplete loss of cerebral regulation of vasomotor function in patients with partial lesions accounts for better circu-

lation. The high incidence of venous block with thoracic complete lesions, on the other hand, may be connected with the lack of cerebral vasomotor regulation.

The relationship between the duration of paraplegia and incidence of venous block showed apparently two peaks within the first, third, and fourth years, respectively. This period must not be interpreted as the exact time at which venous occlusion actually occurred but rather indicates that the block was then first detected. Nevertheless it is important that one-third of the cases of venous occlusion were observed within the first year after injury which coincides with the stormy period well known to those familiar with the course of paraplegia during which homeostasis to physical and mental stress is not yet accomplished.

The majority of our patients consisted of World War II veterans and, therefore, the age of those with block was conspicuously lower (20 to 40 years) than that of patients (50 to 69 years) with postoperative thrombosis as observed by Allen, Barker, and Hines.

The involvement of the left extremity was slightly higher than that of the right (44 to 39) among patients with unilateral and bilateral blocks or even somewhat higher (19 to 14) among those with unilateral occlusion only. Yet, this ratio is much lower than that of patients with postoperative thrombosis (2 to 1) as described by Allen, Barker, and Hines.

Swelling or edema of the lower extremities is not infrequently observed in patients with cord injury; its causes may be manifold. Among our 99 patients, 14 had unilateral or bilateral swelling, but only 10 of them also had a venous block; these 10 cases form 17 per cent of the 58 patients with venous occlusion. Swelling may be, therefore, a diagnostic guide and the only pathognomonic sign. The common symptoms of venous occlusion are practically absent because the neurologic deficit abolishes such features as pain, tenderness on examination, and Homans' sign; while fever, tachycardia, increased sedimentation rate, and malaise may well be caused by pyelitis, decubitus ulcers, or other complications of paraplegia. The positive phlebogram permits the diagnosis of deep occlusion.

TABLE II.—NUMBER AND DISTRIBUTION OF PATIENTS WITH VENOUS OCCLUSION WITH REGARD TO SPASTICITY OR FLACCIDITY

Type of lesion	Spasticity No. cases	Flaccidity No. cases	Total No.
Complete			
C	1	0	1
T	5	31	36
L	0	2	2
Total	6	33	39
Incomplete			
C	2	3	5
T	3	5	8
L	2	4	6
Total	7	12	19
Sum total	13	45	58

C, cervical; T, thoracic; L, lumbar

Whether the cause of swelling was vascular or metabolic no therapy was used other than elevation of the limb. No anticoagulants were administered in paraplegic patients because of the obvious contraindication, namely, trauma of the spinal cord and renal damage. Despite this attitude only 3 cases of pulmonary embolism are known to one of us (E.B.) among more than 1,000 paraplegics observed during an 8 year period; these 3 patients are not included in this series. Two of them showed clinical and x-ray findings of pulmonary embolism but recuperated readily, while the third succumbed 7 years after his original injury, which was caused by a bullet and was followed by flaccid paraplegia below the eighth thoracic dermatome. He was living at home after his discharge from the paraplegia center 5 years prior to and at the time of death. There was no history of illness preceding the fatal pulmonary embolism which was listed as the cause of death in the coroner's necropsy report. The incidence of pulmonary embolism is, therefore, low for a group of 1,000 cases, namely, 0.3 per cent with a mortality of only 0.1 per cent, comparing favorably with the number of deaths from renal dysfunction, calculated as 2 per cent among 844 traumatic paraplegics (2).

SUMMARY

1. Ninety-nine patients with injury to the spinal cord or cauda equina underwent bilateral phlebography of the lower extremities.

2. Fifty-eight patients (58.6 per cent) showed roentgenographic evidence of unilateral or bilateral deep venous occlusion.

3. Venous occlusion was significantly more frequent in patients with flaccid than in those with spastic paraplegia.

4. One-third of all venous blocks were observed within the first year after injury.

5. The highest incidence of occlusion occurred in the veins of the thigh, then in those of the lower leg, and last in the pelvic veins.

6. The left lower extremity was involved somewhat more often than the right.

7. Swelling and edema of the lower extremities were noticed in 14 patients, but only in 10 accompanied by venous occlusion.

8. No anticoagulant therapy was used, yet only 3 cases (0.3 per cent) of pulmonary embolism (not included in this series) have occurred among 1,000 paraplegic patients, with 1 (0.1 per cent) fatality.

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THE SURGICAL SIGNIFICANCE OF REGIONAL LYMPHATIC DRAINAGE OF THE HEPATIC FLEXURE

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VARIANCE of opinion exists regarding the ideal point of ligation of the middle colic artery during the performance of right hemicolectomy for carcinoma of the proximal colon. This is particularly true for lesions in the region of the hepatic flexure.

The difference of opinion centers around two important fundamental issues, namely the desirability of complete extirpation of the regional lymph channels draining a malignant lesion, and the maintenance of an adequate blood supply to the anastomosis and remaining intestine after resection. Those advocating removal of the entire middle colic artery point out that this step is necessary for the removal of the entire middle colic lymph chain. Others have been fearful that removal of the middle colic artery in its entirety would jeopardize the arterial blood supply to the anastomosis and the residual transverse colon, and have compromised with excision of only the right branch of this vessel. Steward and Rankin found the marginal artery to be continuous from the ascending colon to the sigmoid in all but 5 of more than 100 specimens examined, and in these 5 cases, the failure of anastomosis occurred between the ileocolic and right colic arteries. In none of their specimens did they note failure of anastomosis between the left colic and middle colic arteries. These findings suggested that the entire middle colic artery could be safely removed.

From an anatomic viewpoint, the removal of the right branch of the middle colic artery would permit removal of the epicolic, paracolic, and intermediate groups of nodes, but would leave remnants of the main group of nodes in situ.

Because the frequency of metastatic involvement of the main group of middle colic nodes by lesions of the hepatic flexure is unknown, the present study was undertaken. It was hoped also that "tagging" the lymphatics with a vital staining dye would permit identification of the basic patterns of lymphatic drainage from the hepatic flexure.

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Abridgment of portion of thesis submitted by Dr. Phillips to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Master of Science in Surgery.

REVIEW OF THE LITERATURE

The present pattern for radical excision of malignant lesions in the proximal colon was established by Friedrich in 1904, and there is general agreement that his approach for removal of cancer in this portion of the bowel is the procedure of choice. The procedure which Friedrich advocated, and which has come to be implied by the term "right hemicolectomy," is the en bloc resection of a short segment of terminal ileum, the cecum and appendix, the ascending colon and hepatic flexure, and the proximal third of the transverse colon, plus the attached mesentery, blood vessels and regional lymph channels and nodes. Cheever reviewed the rationale of this approach, and stressed the increased margin of safety afforded by resection of a larger segment of colon plus its attendant regional lymphatics.

Prior to the acceptance of Friedrich's approach to this problem, resections for malignant lesions in the right colon had been of a segmental nature, dealing mainly with the tumor-bearing area, and neglecting the channels of regional lymphatic drainage. Death from recurrence of the lesion was a common sequel in patients thus treated, and the recurrence in many instances has been ascribed as glandular.

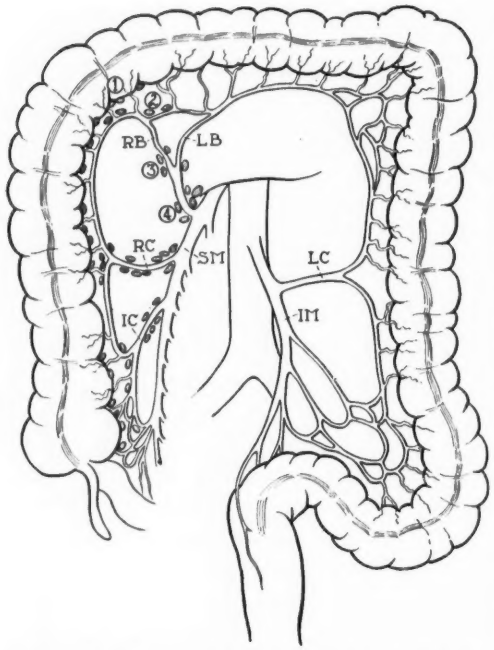

Fig. 1. Lymphatics of right side of colon. *1*, Epicolic nodes; *2*, paracolic nodes; *3*, intermediate group nodes; *4*, main group nodes. Superior mesenteric artery (*SM*); ileocolic artery (*IC*); right colic artery (*RC*); right branch of middle colic artery (*RB*); left branch of middle colic artery (*LB*); left colic artery (*LC*); inferior mesenteric artery (*IM*).

Jamieson and Dobson have described the extramural lymphatic system of the colon as consisting of chains of lymph channels and nodes distributed along the course of the blood vessels. Consequently, these lymphatic chains have been named according to the particular blood vessels they accompany. There is an inferior mesenteric chain, a left colic chain, a middle colic chain, a right colic chain, and an ileocolic chain. Along each chain there are groups or aggregations of nodes which, although they actually tend to merge into one another and are not distinct entities, are designated as the epicolic, paracolic, intermediate, and main groups of nodes (Fig. 1). In general, the lymph flow is directed primarily through the epicolic and paracolic nodes, and eventually to the more centrally located intermediate and main group nodes. However, exceptions to this general scheme of drainage have been reported. Jamieson and Dobson concluded that some middle colic lymphatic channels reach the intermediate group of nodes directly in all cases (that is, without being primarily intercepted by the paracolic nodes), and reach the main group directly in many instances, but only from the ascending and transverse limbs of the hepatic flexure—the lymphatics from the central portion of the transverse colon all being intercepted primarily by the paracolic nodes. Rouvière also believed that some lymphatic channels led directly from the hepatic flexure into the intermediate and main groups of nodes, without primary interception by other nodes.

Grinnell reported that metastatic growths were confined to the epicolic and paracolic nodes in 25 per cent of 322 colonic and rectal lesions examined, but had reached the intermediate nodes in 18 per cent. He noted that no specimen from the right side of the colon showed lymph spread directly to an intermediate node without first involving an epicolic or paracolic node. In the specimens examined by Grinnell, metastasis occurred along the ileocolic route in every right colonic lesion with positive nodes, and the middle colic route was involved only in tumors distal to the hepatic flexure. Coller, Kay, and MacIntyre have reported 2 lesions of the hepatic flexure from which spread occurred along both middle colic and ileocolic lymph chains.

MATERIALS AND METHODS

This study includes patients presenting at the Mayo Clinic for surgical removal of a cancer of the hepatic flexure during an 11 month period (November 1952 through September 1953). No method of selection was employed, and the cases were investigated as they appeared on the surgical schedule for operation. The only requisite for inclusion in this study was that the middle colic artery be ligated at its origin, in order that subsequent evaluation of nodal metastasis in the fresh surgical specimen could include the main group of middle colic nodes, as well as the intermediate, epicolic, and paracolic groups.

In all, five different staff surgeons cooperated in providing 9 specimens for this investigation. No standardized procedure was employed in performing hemicolectomy in these cases, insofar as the individual surgeon decided as to the feasibility of resecting the entire middle colic artery, only after a careful preliminary exploration had been carried out, and he was amply satisfied that such a resection would not jeopardize the blood supply of the ileocolic anastomosis nor the residual segment of transverse colon. It was necessary to exclude only 1 specimen on the basis of incomplete removal of the middle colic artery. In this case, the artery was ligated near its bifurcation, with resection of only its right branch. Actually, the decision not to remove this vessel in its entirety was not based on concern for the anastomotic blood supply, but rather was due to the presence of shock and the poor general condition of the patient.

In order to facilitate the identification of lymph nodes, and with the thought that the basic patterns of lymph drainage might be localized more clearly, the specimens were injected with a vital staining dye, according to the technique employed by Weinberg and associates in the surgery of gastric, pulmonary, and colonic lesions. Pontamine sky blue, an azo dye with desirable vital staining properties, was used for this purpose.

After exploration of the abdomen was completed, a total of 5 cubic centimeters of a 4 per cent aqueous solution of the dye, to which had been added 30 turbidity-reducing units of hyaluronidase, was injected via a small (22 to 24 gauge) needle into the muscularis externa at the site of the lesion. Multiple injections served to distribute the dye around the immediate periphery of the lesion, care being taken to avoid the injection of large vessels. Spillage of the dye over the mesentery and mesocolon was avoided, in order to minimize extraneous patterns of staining, and so as to be assured that any dye appearing in the areas of regional lymph drainage would, of necessity, have been absorbed from the dye deposited at the site of the lesion.

After the injection of dye was accomplished, the resection proceeded in the usual manner.

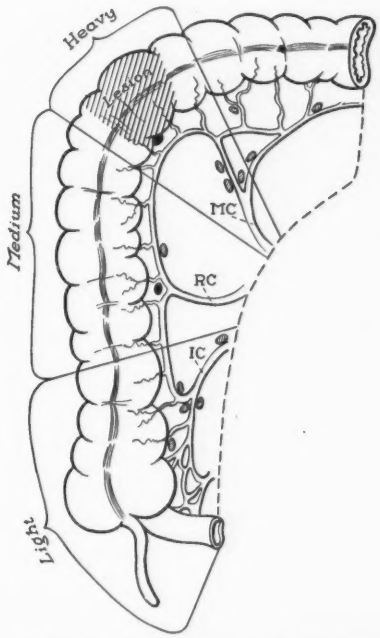

Fig. 2. Grade 2 adenocarcinoma of the hepatic flexure. The lymph nodes examined microscopically in this specimen are depicted by oval-shaped dots. Their position with respect to the major arterial blood supply is indicated. Solid black ovals signify metastatically involved nodes; crosshatched ovals represent microscopically negative nodes. The segments of bowel delimited by brackets and labeled heavy, medium, and light, correspond to the middle colic, right colic, and ileocolic lymphatic channels, and refer to the intensity of staining by the dye injected at the site of the lesion. Thus, in this particular specimen the middle colic lymphatics assumed a very heavy stain as a result of diffusion of the injected dye, while staining of medium intensity was seen in the right colic lymphatics, and staining of a very light intensity was noted in the ileocolic lymphatics. Middle colic artery (*MC*); right colic artery (*RC*); ileocolic artery (*IC*).

It was noted that the dye diffused throughout the regional lymphatics quite rapidly, requiring about 5 to 10 minutes to appear in the main group nodes in the vicinity of the origin of the middle colic artery. The intervening groups of lymph nodes and many of the lymphatic vessels could thus be identified grossly.

In each of the specimens which was injected, the dye had diffused sufficiently so that the lymphatics were adequately outlined before ligation of the main vessels and completion of the resection.

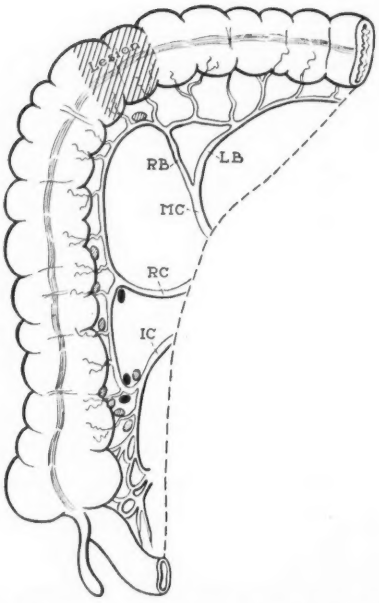

Fig. 3. Grade 2 adenocarcinoma of the hepatic flexure. As described in the text, this specimen showed heavy staining of the right colic lymphatics, and light staining of the ileocolic lymphatics. The middle colic lymphatics were entirely unstained. One right colic and 2 ileocolic lymph nodes were metastatically involved. No lymph nodes were found along the middle colic channel. Right colic artery (*RC*); ileocolic artery (*IC*); middle colic artery (*MC*); right branch of middle colic artery (*RB*); left branch of middle colic artery (*LB*). Black ovals signify metastatically involved nodes; crosshatched ovals represent microscopically negative nodes.

The fresh surgical specimen was taken directly to the surgical pathology laboratory for examination. The specimen was laid out in the approximate contour it had occupied in the abdomen and a diagram was drawn of the resected colon including the relationship to its main vessels. After orientation of the gross specimen as to important relationships, a careful dissection of the lymph nodes was made. Before each node was removed for microscopic examination by the frozen section method, the relative position and distance of the node from the lesion and to the major vascular patterns were noted. A permanent record of the position and relationship of lymph nodes to these structures was made by entering this information on the diagram of the gross surgical specimen.

RESULTS

As mentioned previously, the dye was picked up quite rapidly, requiring approximately 5 to 10 minutes to outline the regional lymphatics. In all 9 specimens injected by this method, the dye had diffused sufficiently throughout the lymphatics accompanying the right branch of the middle colic artery, and the main trunk of this vessel, so that nodes in the epicolic, paracolic, intermediate, and main groups were stained. No lymphatic staining was evident in the region of the left branch of the middle colic artery, except in 1 case, wherein a single, very lightly stained, intermediate group node was found. This node lay equidistant between the origin of the middle colic artery and the wall of the midtransverse colon.

In 7 specimens the dye was taken up by the middle colic lymphatic channel only and did not appear in the ileocolic nor right colic lymphatics. In the eighth and ninth specimens, however, it was evident that the dye had diffused via multiple channels. One of these 2 specimens showed staining of the lymphatics along the middle colic, right colic, and ileocolic arteries, in order of decreasing intensity. That the right colic lymphatic chain drained the region of the carcinoma of the hepatic flexure in this particular case was evidenced by the presence of a metastatically involved paracolic lymph node adjacent to a branch of the right colic artery (Fig. 2). The other specimen in which diffusion of the dye occurred along multiple channels showed a pronounced staining of the right colic lymphatic chain, and a slight staining of the ileocolic lymphatics, while the middle colic lymphatics remained entirely unstained by the dye. The finding of 1 metastatically involved right colic node and 2 ileocolic nodes with metastatic growths further indicated that the right colic and ileocolic lymphatic channels were the major routes of lymph drainage in this particular case (Fig. 3). Our findings in these latter 2 cases are in agreement with the 2 cases reported by Coller, Kay, and MacIntyre, in which metastasis occurred along the middle colic and right colic lymph channels in 1 case, and along the middle colic and ileocolic lymphatics in the other.

A total of 98 lymph nodes were examined in the 9 specimens.

Five of the 9 lesions studied showed grade 2 adenocarcinoma (Broders), and 2 specimens each were of grades 1 and 3. None of the lesions studied were of grade 4 malignancy.

According to the degree of penetration by the lesion (Dukes's classification), 2 were type A, 4 were type B, and 3 were type C.

In the first case with nodal involvement (type C, Dukes) the lesion was of grade 2 with a positive epicolic node adjacent to the lesion, and a second positive paracolic node which was located adjacent to a branch of the right colic artery. This case has been described earlier in this paper to illustrate its unusual pattern of lymphatic drainage (Fig. 2). The second lesion of type C was a grade 2 adenocarcinoma. This specimen contained 1 positive right colic node and 2 positive ileocolic nodes, and its unusual pattern of lymph drainage was previously described (Fig. 3). The remaining lesion of type C was a grade 3 adenocarcinoma, and the specimen contained only 1 positive node. However, the location of this node was of particular interest, since it was situated adjacent to the main branch of the middle colic artery, and central to the main bifurcation of that vessel. It was located 0.5 centimeter peripheral to the point of ligation and division of the middle colic artery at its origin from the superior mesenteric artery (Fig. 4). Thus, here was a metastatically involved node which, by virtue of its location in the main group of middle colic nodes, would have most certainly been left in situ had not a special effort been made to remove the entire middle colic artery. Ligation and removal of only the right branch of the middle colic artery would obviously have fallen short of removing this node.

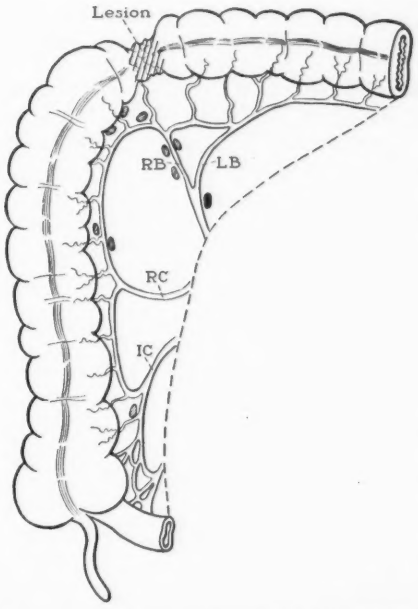

Fig. 4. Grade 3 adenocarcinoma of the hepatic flexure. The dye injected at the site of the lesion in this specimen was taken up entirely by the middle colic lymphatics. No staining occurred in the right colic or ileocolic lymph channels. The single metastatically involved node in this specimen was located in a position corresponding to the main group of middle colic nodes. Crosshatched ovals represent microscopically negative nodes; black ovals signify metastatically involved nodes. Right branch of middle colic artery (*RB*); left branch of middle colic artery (*LB*); right colic artery (*RC*); ileocolic artery (*IC*).

COMMENT

As a result of their anatomic findings, Jamieson and Dobson emphasized the importance of removing the entire middle colic lymphatic chain for lesions in the region of the hepatic flexure, and stated that the fulfillment of this precept entails ligation of the middle colic artery at its origin from the superior mesenteric artery, with the removal of the mesocolon from this point up to the bowel. This step permits complete extirpation of the entire middle colic chain of lymph nodes. High ligation of the middle colic vessels in resecting lesions of the hepatic flexure and proximal transverse colon has also been advocated by Gilchrist and David, Grinnell, Mayo and Schlicke, Mayo, McKittrick, and Person and O'Neill. However, Coller, Kay, and MacIntyre advocated removal of only the epicolic, paracolic, and intermediate groups of nodes in resection of malignant lesions of the colon. In their opinion, metastatic involvement of main group nodes would signify that generalized metastasis had occurred, and, therefore, any surgical procedure would necessarily be of a palliative nature.

The incidence of metastasis from colonic lesions directly to the main group of nodes is not known, but is probably small. It is known, however, that the main group of middle colic nodes is situated at the origin of the middle colic artery, and is proximal to the main bifurcation of that vessel. Resection of only the right branch of the middle colic artery falls short of complete extirpation of the entire middle colic lymph chain, in that it does not entirely remove the main group of nodes. Consequently, the main group of nodes in the middle colic chain is frequently out of reach of the usual surgical excision.

Some unusual variations in the middle colic artery have been recorded. Steward and Rankin concluded that the middle colic artery does not occur constantly, and that through large branches or by accessory middle colic arteries, it supplies the left side of the transverse colon and splenic flexure in about 37 per cent of cases. Sappey stated that the middle colic artery is often absent. In 4 per cent of specimens examined by Steward and Rankin, this vessel was entirely absent, and was replaced by a large branch of the left colic artery. Moynihan and Jamieson and Dobson occasionally noted an accessory middle colic artery running directly toward the middle of the transverse colon. In 10 per cent of specimens Steward and Rankin found an accessory middle colic artery arising from the superior mesenteric artery above the origin of the middle colic, and running to the left in the mesocolon to anastomose with the marginal artery near the splenic flexure. The relative constancy of the marginal artery in the region of the transverse and descending colon, as noted by Steward and Rankin, was mentioned previously. Thus, in spite of anatomic variations in the middle colic artery, ligation and division of this vessel at its origin should be possible in most instances, without fear of jeopardizing the blood supply to the ileocolic anastomosis or the remaining portion of colon.

The basic pattern of lymph drainage from the hepatic flexure, as outlined by vital staining in this investigation, is in agreement with and would tend to corroborate the report by Coller, Kay, and MacIntyre, that metastatic growths may occur along the middle colic, right colic, and ileocolic lymph chains from lesions in this location.

Although metastasis from lesions of the hepatic flexure directly to the main group of middle colic nodes is probably rare, it occurred in 1 specimen in this study. This finding supports the contention of Jamieson and Dobson, that some lymph channels drain directly from the hepatic flexure into the main group of nodes at the point of origin of the middle colic artery, without being primarily intercepted by the intervening groups of nodes.

Because of the anatomic and pathologic variations encountered in lesions of the hepatic flexure, standardization of technique in removal of these lesions is as undesirable as it is impossible to achieve. However, because of the possibility of even occasional metastasis from a lesion of the hepatic flexure to the main group of middle colic nodes, it would seem that the performance of an adequate resection necessitates removal of the main group nodes, as well as the epicolic, paracolic, and intermediate groups, whenever feasible. Certainly, this complies with the tenets of good cancer surgery from the standpoint of complete extirpation of regional lymphatics.

Although the number of lesions studied in this investigation is relatively small, the cases available for such a study are scarce, owing to the low incidence of malignant lesions in this segment of the colon. We are mindful of these considerations in offering the following conclusions.

CONCLUSIONS

1. The lymphatic chain accompanying the right branch of the middle colic artery is the major route of lymph drainage from the hepatic flexure, and as such, can logically be expected to be the main route of lymphatic metastasis for lesions in this segment of the colon.

2. In some cases, the right colic and ileocolic channels also drain lymph from the hepatic flexure, but the present study suggests that these routes are of secondary importance in this respect.

3. Removal of only the right branch of the middle colic artery does not completely extirpate the middle colic lymph chain. Consequently, the main group of nodes is often out of reach of the usual surgical excision.

4. Removal of the entire middle colic artery in the course of right hemicolectomy for lesions of the hepatic flexure should be accomplished in the majority of instances, without fear of jeopardizing the blood supply to the ileocolic anastomosis or to the residual portion of left transverse colon.

5. Because of the ease and relative impunity of extending the scope of a right hemicolectomy in this manner, and because of the possibility of metastatic involvement of the main group of nodes, the procedure should ideally include ligation of the middle colic artery at its origin, with the removal of the main group of middle colic nodes, whenever feasible.

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CLINICAL APPLICATIONS OF OBSTETRIC RADIOLOGY

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ALTHOUGH the literature contains many papers concerning some particular phase of obstetric radiology, there have been relatively few dealing with the broad clinical integration of the two specialties. It is our belief that there is not sufficiently widespread recognition of the valuable contributions x-ray studies have to offer in the field of obstetrics, and that the many applications of this important diagnostic aid are not fully utilized.

The material here presented has its origin in the obstetric radiology conferences conducted at the University of Michigan Hospital. At these conferences, films taken during the preceding week are reviewed after a brief presentation of the pertinent history of each case. They are interpreted jointly by roentgenologist and obstetrician. Since the conference is held weekly, there is ample opportunity for follow-up on all cases presented. The value of such a co-operative effort is indicated by the popularity of the conference, even at 8:00 a.m., among both staff members and medical students. It cannot be overemphasized that the one factor which has been vital to the continuing success of this conference is the atmosphere of co-operation between members of the two departments. Problems are approached with the thought that both can learn something and the interchange of ideas has been most rewarding. The joint discussions serve to emphasize repeatedly that information gained from x-ray studies is only a part of the whole picture and must be integrated with clinical findings. In addition, the obstetric residents gain a certain familiarity with film interpretation and thus avoid the common pitfall of placing too much reliance on a typed x-ray report. Similarly, the radiology residents gain some insight into the problems faced by the obstetrician.

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Since the opening of the new Women's Hospital in February, 1950, the convenience of having a well equipped, adequately staffed, and easily accessible x-ray unit has led to an increasing use of these facilities. While some of these examinations may not have been essential to the management of a given case, they have added immensely to our understanding of certain obstetric problems.

RADIOGRAPHIC CONSIDERATIONS

The radiographic examination of the obstetric patient can be carried out with the standard equipment of any x-ray department. Various modifications have been developed to improve or facilitate the examination. In general, the exposure factors necessary are 75 to 95 kilovolts and 150 to 500 milliampere seconds.

To satisfy ourselves that the amount of radiation received by a fetus during our routine radiographic examination of the mother is within acceptable limits, we have made a series of direct measurements. A Victoreen thimble chamber and various ionization chambers were placed against the cervix and on the skin of the pregnant abdomen during these exposures. By inserting a rubber covered Victoreen thimble chamber into a colostomy stoma of a nonpregnant patient, measurements were also made of the radiation delivered to the center of the abdomen. With our equipment and an added filter of 0.5 millimeter of aluminum to reduce the soft radiation, it was estimated that the fetus received about 0.1 roentgen for each frontal exposure and from 0.2 to 0.3 roentgen for each lateral exposure. Thus, in our routine examination, the fetus probably receives a total of less than 1 roentgen. Since most radiographic examinations are conducted during the latter part of pregnancy, we believe that this order of dosage is within the limits of safety, both with respect to direct effect on the fetus and the possible genetic effect.

A number of special positions and techniques have been devised for the roentgen study of obstetric problems. These are based on years of experience and the contributions of many workers in this field. With and without accessory apparatus for immobilizing the patient and recording devices for subsequent measurements, various views of the abdomen, pelvis, pelvic inlet, and subpubic arch have been described. In order to reduce their complexity and to have a routine applicable to the majority of obstetric problems that arise, we have evolved a standard set of films. Thus, obstetricians, radiologists, technical and secretarial personnel refer to the "obstetric routine" with a mutual understanding of what constitutes this minimum film study. The bladder is emptied routinely prior to x-ray examination to avoid confusing displacement of the fetal head. The routine exposures are then made as follows:

1. A 14 by 17 inch anteroposterior supine frontal film centered 1 inch above the iliac crest so as to include the entire uterus and the maternal pelvis (Fig. 1).

2. A 14 by 17 inch lateral film of the abdomen centered 1 inch above the iliac crest to include the entire abdominal wall, the entire uterine contour, and the lumbar spine. A wedge filter made of radiopaque plastic is used for this exposure. The thickest part of the wedge reduces the exposure in the region of the soft tissues of the anterior uterine and abdominal walls. The thin edge of the wedge is over the midaperture of the tube, leaving the unaltered beam for exposure of the posterior uterine wall and lumbar spine. In this way, excellent soft tissue detail of the entire uterine wall, in lateral projection, is obtained (Fig. 2).

3. A 10 by 12 inch lateral projection of the maternal pelvis, centered 1 inch above the greater trochanter and including the entire pelvis, is then obtained for a qualitative estimate of anteroposterior pelvic diameters and their relations to the fetal head (Fig. 3).

These 3 films afford all the roentgen information necessary for the great majority of obstetric problems. Problems of fetal age, development, position, death, placental localization, multiple pregnancies, hydramnios, and the qualitative evaluation of cephalopelvic relationships can be adequately studied by this minimum 3 film routine. For precise pelvimetry, a 10 by 12 inch frontal film, centered 1 inch above the pubis, is added.

Precise radiographic pelvimetry can be accomplished by any of several methods. The specific means by which the distortion, inherent in roentgenograms, is corrected is unimportant if the method is understood and properly used. There is little need to be concerned with fractions of centimeters in dealing with pelvic measurements when the endpoints of the diameters are themselves uncertain and when important clinical factors have such a wide range of variability which cannot be precisely assessed. We make no attempt to classify a pelvis according to any of the several systems, but try to estimate whether each of the 3 major planes—inlet, midplane, and outlet—is adequate for the safe passage of the fetus currently in utero.

Most recently we have used a system of pelvimetry described by Hodges and Nichols[1] and known as orthographic pelvimetry. It requires a special table on which the tube, cassette holder, and grid are mounted on a cradle which can be rotated through 90 degrees about the pelvis. In this fashion, excellent frontal and lateral projections can be obtained without moving the patient. With this method, frontal and lateral films of the pelvis are used to provide corrected tracings from which direct measurements can be made. After the films are dry, the time required to obtain the measurements is brief. We have found that the pelvimetry films are more informative when viewed in association with large frontal and lateral views of the abdomen. As a result of our attempt to evaluate all of the factors involved in the process of delivery, we have learned that the necessity for pelvimetry studies has decreased markedly.

APPLICATIONS OF X-RAY EXAMINATIONS DURING PREGNANCY

There are many situations in the care of obstetric patients in which radiographic examination is helpful. Proper integration of the clinical and radiographic findings provides a sound basis for determining the most effective management in many obstetric problem cases. As our familiarity with x-ray examina-

[1]HODGES, P. C., and NICHOLS, R. L. Orthographic pelvimetry. Radiology, 1949, 53: 238.

TABLE I.—INDICATIONS FOR X-RAY EXAMINATIONS DURING PREGNANCY

	Per cent of total
Estimation of fetal age	27.7
Placental localization	20.3
Evaluation of fetopelvic size relations	17.7
Evaluation of the atypical pregnant abdomen	14.8
Study of abnormal labor	10.6
Evaluation of fetal position, presentation, and attitude	4.2
Determination of fetal death or abnormality	3.2
Confirmation of pregnancy	1.3

tion of the pregnant patient has increased, so has the scope of its usefulness. In an unselected series of several hundred consecutive cases, the indications for obtaining roentgen study were as listed in Table I. It has not been our policy to obtain routine pelvimetry on all primiparas. However, maternal chest and newborn survey films are routine in this clinic.

Brief comment is in order on the integration of radiographic and clinical factors in each of these groups.

Maternal chest survey. It is agreed that a thorough physical examination is an essential part of prenatal care. An important aspect of such an examination is a roentgenogram of the chest. In common with other chest survey procedures, this has the objective of detecting intrathoracic abnormalities, thus facilitating their early treatment. If the abnormality is active pulmonary tuberculosis, its discovery aids in preventing unnecessary exposure of the patient's family and the hospital staff. It is especially important that active pulmonary tuberculosis, if present, be discovered during the antenatal period. Institution of treatment at this time may allow adequate control of the disease before delivery. Collapse measures may be augmented by the elevation of the diaphragm occurring in the latter months of gestation. Finally, if under proper care, the patient can be protected during the dangerous postpartum period when spread of the disease is most likely to occur. Such postpartum exacerbation might lead to serious exposure of especially vulnerable infants and children. Aside from pulmonary tuberculosis, other pulmonary disease and cardiovascular abnormalities may be detected and appropriate management carried out.

Neonatal survey. One of the functions of our obstetric radiology unit is to make routine chest films on newborn infants. On either the fourth or fifth day of life, 2 frontal exposures of the infant's trunk are made on a single divided film in an effort to obtain at least 1 in inspiration.

The value of this survey is still to be determined. Interesting variations in mediastinal contour have been noted. Although many congenital heart lesions cannot be recognized at this stage, we have discovered a few by this means. Unsuspected fracture of the clavicle and persistent fetal atelectasis have also been found. The neonatal survey films have occasionally proved helpful in evaluating subsequent disease. In general, the most significant value of this survey has been the demonstration of the wide variation in the appearance of the normal newborn chest.

Estimation of fetal age. The estimation of fetal age is important in several clinical situations. The accuracy of its determination by roentgen methods increases as the fetus approaches maturity. When one is contemplating artificial induction of labor or cesarean section in such complications as diabetes, certain Rh incompatibilities, repeat cesarean section, or toxemias, it is important to consider the maturity of the fetus. In these instances, it is equally desirable to avoid terminating pregnancy when the baby might suffer the hazards of prematurity and to avoid the increasing risks of prolonging the pregnancy. Roentgenograms may also provide the basis for revising an originally erroneous expected date of delivery, thus giving reassurance to both patient and physician.

From a radiologic standpoint, there are only 2 ossification centers of practical value in determining fetal maturity. These are the distal femoral epiphyses which usually appear at about 35 to 36 weeks of gestation, and the proximal tibial epiphyses which ossify 3 to 4 weeks later. If we can identify either or both of these centers on the obstetric routine films, there is excellent assurance that the pregnancy has progressed to a stage where the chances for extrauterine survival are good.

Additional helpful signs of fetal maturity are the presence of a well developed subcutaneous fat line, usually best seen on the lateral film of the obstetric routine, and a well calcified fetal skull. Other indices of fetal maturity have not proved practical in our experience.

Again it should be emphasized that these specific criteria are most valuable when correlated with the over-all size of the fetal skeleton and the clinical estimation of fetal age.

Placental localization. One of the most frequent indications for x-ray examination of the obstetric patient is vaginal bleeding during the last trimester of pregnancy. In this situation the urgent problem is the confirmation or exclusion of placenta previa, and roentgenograms can be of extreme value. The position of the placenta is indicated by a soft tissue shadow of uniform density, lying between the subcutaneous fat line of the fetus and the external uterine contour, which is in excess of the width of the uterine wall alone. This is frequently seen to best advantage in the lateral projection (Fig. 2) and normally the greatest thickness of such a placental shadow is at or above the midportion of the uterus. This evidence of a normally situated placenta excludes the possibility of placenta previa. In our experience, calcification within the placenta has not been helpful in its roentgen localization. In addition to the observation of the placental site, the relation of the presenting part to the maternal pelvis should be evaluated. Normally, the fetal skull is approximately equidistant from the boundaries of the pelvic inlet as seen in both frontal and lateral projections. A similar but less precise relationship also applies to breech presentations. Any displacement of the presenting part from this normal relationship within the maternal pelvic inlet should lead one to suspect the presence of a low-lying placenta. This finding carries additional weight if a normal placental site cannot be identified or if there is additional soft tissue evidence of a low-lying placenta. In some instances, these findings may even permit the diagnosis of an asymptomatic placenta previa. It is imperative that the bladder be emptied when these films are taken and highly desirable that the rectum also be empty, since either a full bladder or rectum may displace the presenting part. We have not been impressed that gravity is a significant factor in determining the relationship of the fetal head to the maternal pelvis, and in our experience the obstetric routine films made with the patient in the horizontal position have been entirely satisfactory.

Fig. 1. Obstetric routine film 1: frontal projection of abdomen and pelvis.

An occasional helpful feature in the identification of placenta previa is the persistence of an abnormal presentation. In these cases, the absence of soft tissue contours of the placenta in the upper portion of the uterus lends further weight to the presumptive diagnosis of placenta previa.

The use of contrast material within the bladder is occasionally helpful in demonstrating interposed soft tissue between the bladder and the fetal head. However, with adequate soft tissue films taken after preliminary emptying of the bladder, we have found little need for such contrast studies.

It may be that stringent application of these criteria will suggest placenta previa in a few cases in which the diagnosis is not verified. In

Fig. 2. Obstetric routine film 2: lateral projection of abdomen, demonstrating high posterior placenta, and full term fetus.

any event, it is better to have further clinical investigation exclude these few cases than to overlook such an important obstetric complication. The roentgen examination in cases with bleeding is most helpful in the subsequent management of the patient. If the placenta can be definitely localized in the upper portion of the uterus and if there is no displacement of the fetal head with respect to the pelvic inlet, we believe that placenta previa can be excluded and that digital palpation through the cervix can be omitted. However, the cervix should be inspected, since a local cervical source of bleeding may be present. By thus relying on roentgenograms to exclude placenta previa, the possibility of premature induction of labor is avoided. If, on the other hand, the x-ray signs are suggestive of placenta previa, then proper clinical evaluation is necessary. Digital palpation through the cervix may be indicated if the patient is near term or if bleeding is sufficient to demand immediate intervention. Thus, the roentgen findings aid in the selection of cases necessitating further clinical examination. As our experience with placental localization has increased, we have been able to reduce considerably the number of patients requiring sterile vaginal examination to exclude the presence of placenta previa.

In a recent analysis of a significant number of our patients examined radiographically because of bleeding during late pregnancy, placenta previa was suspected in 22 per cent of the cases. The diagnosis was verified clinically in approximately one-half of these. In the remaining 78 per cent of the series, it was possible definitely to rule out placenta previa by the obstetric routine roentgenograms. The subsequent clinical course verified the roentgen exclusion of placenta previa in every patient. We believe it is important to emphasize that not 1 case of placenta previa has been missed by roentgen examination.

Evaluation of fetopelvic size relations. Evaluation of the possibility of safe vaginal delivery requires consideration of the pelvic canal, the fetus, and the uterine contractions. Since the largest and the most unyielding part of the fetus is the head, our problem is primarily one of determining the cephalopelvic relations.

By appropriate x-ray studies, the various pelvic diameters can be measured accurately to within a few millimeters. Several satisfactory methods are available. However, in our experience, rotation of the fetal head and distortion of its image preclude its accurate measurement. It seems illogical to be so precise about the pelvis and so inaccurate about measurement of the fetal head. In our opinion, an unwarranted amount of attention has been directed toward the precise measurement and classification of the maternal pelvis. Consequently, we are now using x-ray pelvimetry only on rare occasions. We do not believe roentgen pelvimetry is necessarily essential to the proper management of any given patient. By combined radiologic and obstetric interpretation of the films in cases of questionable disproportion, we are usually able to anticipate the plane of the pelvis where difficulty may be expected, and to estimate the degree of disproportion. This information permits us to proceed with a more intelligent test of labor than would otherwise

be possible. Safe vaginal delivery requires a favorable combination of pelvic size, fetal size, fetal position, fetal head moldability, and uterine contractions and all must be appropriately evaluated. Therefore, we believe that cesarean section is rarely justified solely on the basis of x-ray evidence of disproportion.

Evaluation of the obstetrically atypical abdomen. Several problems in diagnosis fall under this heading: (1) cases in which the uterus is larger or smaller than the menstrual history would indicate, suggesting the possibility of multiple pregnancy, hydatid mole, error in determination of due date, or missed abortion; (2) supposedly pregnant patients in whom the configuration of the abdomen suggests the possibility of associated uterine tumors, or anomalies, or ovarian tumors; (3) patients in whom the abdominal enlargement corresponds with the history but no fetal heart or movement can be detected, suggesting the possibility of hydatid mole, fetal death, or pseudocyesis; and (4) cases of hydramnios, which suggests the possibility of fetal anomaly.

Information gained from the obstetric routine films is usually sufficient to solve these problems or, at least, to contribute materially to their clarification.

Study of abnormal labor. It is well to remember that in the majority of patients, labor progresses in a normal predictable fashion. However, there are occasional patients in whom labor does not progress as we anticipate it should. These are the patients in whom our manual estimation of fetal and pelvic size has permitted a forecast of normal labor but who do not make satisfactory progress. There are three main possibilities which may account for the poor progress and these may sometimes coexist: (1) unrecognized fetopelvic disproportion; (2) abnormalities of presentation, position, or attitude; (3) inertia.

Inertia can, of course, be diagnosed by careful observation of the patient. However, the other factors may not be detectable without the aid of x-ray examination. Films of the obstetric routine will give the necessary information to permit accurate appraisal of the situation so that proper management can be based upon complete knowledge of the factors involved.

Fig. 3. Obstetric routine film 3: lateral projection of pelvis.

Evaluation of fetal position, presentation, and attitude. One occasionally encounters patients in whom it is difficult or impossible to determine clinically the exact fetal lie or in whom the fetus is persistently in some abnormal presentation. Roentgenograms will usually permit accurate assessment of the exact positional relations between fetus and mother, and, in addition, will sometimes suggest the associated cause of the abnormality—such as placenta previa, uterine anomaly or tumor, fetal anomaly, or unsuspected multiple pregnancy.

Determination of fetal death or abnormality. Under various circumstances, the clinician may question whether or not the fetus is living. Clinical findings suggestive of fetal death include: cessation of fetal movement, absence of fetal heart tones, and lack of progressive uterine enlargement. Supportive evidence may be obtained from the roentgenograms of the obstetric routine by observing one or more of the following signs: (1) fetus smaller than the menstrual history would indicate; (2) lack of change of fetal position or attitude over a period of time; (3) apparent compression of the fetus with hyperflexion and sometimes

acute angulation of the fetal spine; (4) persistent deviation of fetal attitude from the normal one of flexion—commonly seen in association with hydramnios; (5) overriding of the skull bones; (It must be remembered that this sign may be observed in living fetuses during labor. Less frequently it is seen in living immature fetuses independent of labor. The overlapping of the bones must be both excessive and persistent before it assumes significance.) (6) relative decrease in density of fetal bones.

It must be remembered that an interval of 1 to 2 weeks following fetal death may be necessary before these roentgen signs become apparent. It is also important to bear in mind that these signs are generally presumptive and a combination of two or more enhances the accuracy of the diagnosis appreciably. The careful integration of clinical findings and roentgen signs should preclude the tragedy of assuming fetal death, inducing labor, and delivering a *living*, premature infant.

Fetal abnormality may be suggested clinically by the presence of hydramnios, inability to palpate the normal fetal parts (particularly the head), or palpation of obvious abnormalities such as hydrocephaly. These suspected abnormalities may frequently be confirmed or excluded by appropriate roentgen study (the obstetric routine). It must be emphasized that fetal abnormality can usually be detected only when there are major bony defects. The most readily detected abnormalities are anencephaly and hydrocephaly. Anencephaly is indicated by absence of the cranial vault, the head being represented by a poorly defined, bony mass. Hydrocephaly is suggested by a disproportionately large head, unusually thin bones in the cranial vault, and, perhaps, abnormal presentation of the fetus since the head cannot enter the pelvis. Other anomalies such as deformities of extremities and spine are less common. Anomalies of the palate, lips, and some minor ones of the extremities are difficult or impossible to diagnose radiographically.

Confirmation of pregnancy. The radiographic detection of pregnancy depends upon the presence of sufficient calcification of the fetal skeleton to cast a shadow on the film. This generally is possible by 4½ months of gestation, although fetal movement, thick panniculus or hydramnios may delay the time of positive recognition. Occasionally, a lateral projection will reveal a fetal skeleton which has been obscured in the frontal film by the heavier maternal bony structures. It is obvious that biologic tests are applicable much earlier and are more practical for early pregnancy diagnosis. However, there are certain cases in which x-ray examinations are very helpful in differentiating between normal pregnancy and various pelvic tumors or abnormal pregnancy.

SUMMARY

From our experience with obstetric radiography, we believe that the following points should be emphasized:

1. There is a great deal to be gained by both obstetrician and radiologist from a cooperative effort in reviewing films taken during pregnancy.

2. Any necessary or indicated x-ray examination can be carried out during pregnancy with complete safety for both the mother and the baby.

3. We have found the use of a 3 film obstetric routine entirely adequate for almost every obstetric problem requiring radiologic examination. We would like to emphasize its simplicity and value.

4. The use of a wedge filter while making a lateral exposure of the abdomen has improved the quality of these films a great deal.

5. In our opinion, radiographic pelvimetry is rarely necessary in the solution of obstetric problems.

6. By our obstetric routine examination, it has been possible to exclude placenta previa in 78 per cent of patients with bleeding in late pregnancy. In no instance has placenta previa escaped detection by this method of examination.

7. As one becomes familiar with the applications of radiology to obstetrics, the scope of its usefulness gradually increases.

LATE RESULTS OF BLADDER SUBSTITUTION WITH ISOLATED ILEAL SEGMENTS

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THE development of pelvic exenteration has focused attention upon bladder substitution by methods other than ureterosigmoidal anastomosis. Until the therapy of cancer of the cervix and uterus is more successful the operation of pelvic exenteration will play a role in their treatment, and the need for a method of substituting for the urinary bladder in the absence of the rectum will exist. Furthermore, the many complications attendant upon ureterosigmoidal anastomosis have led to a distinct need for an improved method of urinary diversion in the treatment of cancer of the urinary bladder and of congenital anomalies. The use of isolated segments of the terminal ileum to convey the urine from both ureters to an external stoma has been practiced by us for a little over 3½ years. Although this period of time is inadequate to determine final end results, sufficient data have accumulated since the initial reports (1, 2, 3) to permit a more detailed analysis than was possible heretofore. The use of isolated segments of terminal ileum as a bladder substitute is technically simple; it is attended by few early and late complications; and the patients are satisfied with this method of urinary drainage.

Table I includes data previously reported (3) as well as more recent cases. Thirty-two of the operations were performed at the Ellis Fischel State Cancer Hospital in Columbia, Missouri, by John Modlin and Henry Schwartz. The other operations were done at the Barnes, St. Louis City, St. Luke's, and Missouri Baptist Hospitals in St. Louis by one of us.

Unfortunately, the evaluation of ileal bladder substitution is complicated by two factors; namely, it is performed usually with other procedures such as cystectomy or pelvic evisceration; and, the postoperative course is complicated frequently by the continuance of the individual's primary disease—carcinoma.

The 106 operations listed in Table I include all cases of ileal segment bladder substitutions performed in the hospitals named. Of these 106 individuals, 65 lived for 6 months or more, and 46 are still alive (July 1, 1953). Nineteen died after living for 6 months or more after the bladder substitution.

The analysis of the efficacy of the ileal bladder devolves upon the observations pertaining to the 65 individuals who lived at least 6 months and those now still living. The data from 46 individuals now living are presented separately in Tables VII and VIII; these represent information obtained by follow-up examination between the dates of January 1 and July 1, 1953.

Death prior to discharge from the hospital is listed as an operative one (Table II). The operative mortality incident to the bladder substitution alone cannot be determined. The last 5 deaths listed in Table II seem directly attributable to it. However, since all of these deaths occurred in the group of patients upon whom a pelvic exenteration had been performed concomitantly, it is possible that the exenteration and not the bladder substitution was the primary lethal factor. On the other hand, it is possible that the other operative deaths, not obviously caused by bladder substitution, may have been due indirectly to this procedure through extension in operating time or by some other manner. For these reasons, the immediate mortality risk of bladder substitution itself cannot be stated accurately. However, there were no operative deaths in the group of 25 patients upon whom ileal bladder substitution was performed without the conduct of an associated pelvic exenteration.

The complications of the bladder substitution itself which caused 1 death in each

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TABLE I.—BLADDER SUBSTITUTION WITH ISOLATED ILEAL SEGMENTS IN 106 PATIENTS

Procedures		No. of cases
With pelvic evisceration		81
With cystectomy		16
Palliative for carcinoma or for fistula		8
For incontinence (myelomeningocele)		1
Available for study of late complications*		65
Not available for study of late complications		41
Operative deaths	15	
Less than 6 months postoperatively	11	
Dead of recurrent cancer less than 6 months postoperatively	3	
Dead of complications of bladder substitution (4 mos.)	1	
Dead of recurrent cancer more than 6 months postoperatively but follow-up incomplete	9	
Alive over 6 months postoperatively but follow-up incomplete	2	
Dead after 6 months follow-up period		19
Recurrent cancer	17	
Unknown cause	2	
Living available for continued study of late complications		46

*Includes all patients with complete data surviving 6 months or longer after bladder substitution.

instance (Table II) were as follows: (1) disruption of the ileoileal anastomosis; (2) disruption of the ileoileal and ureteroileal anastomosis; (This is the only patient in the entire series who developed a ureterourinary fistula after ureteroileal anastomosis.) (3) urinary fistula secondary to the retraction of a poorly made external ileostomy stoma; (4) bilateral ureteral obstruction; (In this instance both ureters had been brought through the mesentery and anastomosed to the anteriorly lying ileal segment; subsequently, the ureters were found to be obstructed at their point of passage through the mesentery. The patient died following an attempted correction of the ureteral obstruction.) (5) acute bilateral pyelonephritis. (This patient, reported previously—2, 3—had infected hydronephrosis with Proteus vulgaris prior to the performance of the pelvic exenteration and bladder substitution. She might have been saved by the performance of preliminary nephrostomy or preliminary bladder substitution by itself.)

TABLE II.—OPERATIVE DEATHS

Dead in first 24 hours from shock	5
Cerebrovascular accident	1
Intestinal obstruction, with fecal fistulas resulting from operative intervention	1
Peritonitis and bronchopneumonia	1
Death from causes unknown with clinical picture dominated by convulsions	2
Fecal fistula (disruption of ileoileal anastomosis)	1
Pyelonephritis, fulminating	1
Urinary and fecal fistulas (from ureterointestinal anastomosis)	1
Urinary fistula and infection from retracted ileal segment	1
Urinary suppression from obstruction of both ureters	1
Total	15

Complications which occurred in this group of patients before discharge from the hospital are listed in Table III. Apparently, many of the complications can be considered as referable to the associated procedure rather than to the bladder substitution: (1) the intestinal obstructions are as readily relatable to the pelvic exenteration as to the reconstruction of the bladder; (2) the 5 significantly infected perineal wounds are attributable to the pelvic exenteration; (3) the 2 pelvic abscesses occurred after cystectomy; (4) the 2 instances of sacral plexus injury which involved the first cord of the plexus and resulted in common peroneal nerve paralysis are attributable to exenteration (1 of these patients is not disabled and has lived for 3½ years); (5) the 1 death from peritonitis occurred in an elderly man who bore a carcinoma of the rectum, and in whom the necessity for a pelvic exenteration was not anticipated, and therefore, the operation was done without adequate preparation of the bowel; (6) 1 massive postoperative hemorrhage requiring immediate reoperation is attributable to the pelvic exenteration alone.

Early nonlethal complications attributable to the bladder substitution are: (1) 5 convulsive states (2 fatal) which may have had as cause some unrecognized fluid or electrolyte disturbance; (2) 3 instances of bilateral progressive hydronephrosis in which the pyelograms obtained 2 weeks after the operation showed hydronephrosis and subsequent pyelograms showed no improvement at the time of discharge from the hospital.

The early complications in 25 patients following bladder substitutions associated with operations other than pelvic exenteration consisted of pelvic abscess in 2 cases and fecal fistula (rectal) in 1 case with no operative deaths.

LATE COMPLICATIONS

The late complications occurring in the 65 patients studied are listed in Table IV. Stenosis of the ileostomy stoma is of minor importance and is easily corrected by operative revision under local anesthesia. In 1 patient stenosis was not recognized until bilateral hydronephrosis had resulted (patient B.H., Table XV). Patients are now instructed to bring a clean bag and glue to the follow-up clinic in order to insure inspection of the stoma at regular intervals. Sensitivity of the skin to the glue used to hold the ileostomy bag in place was a distressing complication which occurred in 1 patient. This problem has not been solved satisfactorily. The patient was in the terminal stage of advanced carcinoma of the bladder and was managed with a Foley catheter in the ileal segment until death. Two patients passed small calculi from the ileostomy stoma, 1 patient having had typical renal colic and microscopic hematuria. Whether this is a complication due to the method of bladder substitution is unknown. However, its occurrence has led us to abandon the use of nonabsorbable suture material in the mucosal layer of the anastomosis because of the possibility of its acting as a nidus for the formation of stone. Eighth nerve injury from streptomycin therapy was a minor complication in 2 patients.

CLASSIFICATION OF LATE RESULTS

The same criteria as previously reported (3) have been used for determining the satisfactory and unsatisfactory results of ileal segment bladder substitution, with the exceptions described in the following outline:

CLASSIFICATION FOR RESULTS OF BLADDER SUBSTITUTION (6 months' minimum follow-up)

Classification by individual renal units (intravenous pyelograms)
- Normal (or 0)—Normal intravenous pyelogram
- Grade I (or 1)—Minimal hydronephrosis
- Grade II (or 2)—Definite hydronephrosis
- Grade III (or 3)—Massive hydronephrosis
- Grade IV (or 4)—Nonfunctioning kidney by intravenous pyelograms

Classification by individual patient (intravenous pyelograms plus clinical evidence of pyelonephritis)

Satisfactory—Those patients never having had clinical evidence of pyelonephritis and with pyelograms showing no worse than grade I hydronephrosis on either side.

Unsatisfactory—All patients having at any time in their clinical course shown evidence of pyelonephritis or with pyelograms showing hydronephrosis of grade II or worse on either side. Exceptions: (1) patients having a nonfunctioning (grade IV) kidney preoperatively which never regains function, if the other kidney is satisfactory and if pyelonephritis never develops; and, (2) patients with satisfactory pyelograms who have had an episode of pyelonephritis in the early postoperative period, but in whom an interval of 1 year or more has passed without subsequent infection.

TABLE III.—EARLY* COMPLICATIONS IN 106 PATIENTS

No. of complications		No. of deaths
Intestinal obstruction (reoperation in 2 patients)	15	1
Thrombophlebitis	6	
Fecal fistula	5	1†
Infected perineal wound	5	
Pelvic abscess	2	
Convulsions (cause undetermined)	5	2
Pyelonephritis	4	1
Progressive bilateral hydronephrosis	3	
Cerebrovascular accidents	2	1
Sacral plexus injury	2	
Pulmonary embolus	2	
Urinary fistulas	2	2
Peritonitis	1	1
Anuria (obstructive)	1	1
Massive postoperative hemorrhage	1	
Operative shock	5	5
Totals	61	15

*Before discharge from hospital; 40 patients had 61 early complications.
†An additional patient had fecal fistula with associated urinary fistula (see Table II).

We have included in the satisfactory category those patients with normal or grade I pyelograms who have had only 1 episode of chills and fever diagnosed as pyelonephritis, but in whom there has been no recurrence of these symptoms for over a year. Five patients are so classified (Table VIII).

Of the 21 patients whose condition is listed as unsatisfactory because of pyelonephritis or hydronephrosis, the 9 with hydronephrosis alone have been completely without symptoms referable to the urinary tract and those surviving their malignant lesions have quite satisfactory clinical results at the present time.

TABLE IV.—LATE* COMPLICATIONS IN 65 PATIENTS

Stenosis of ileostomy stoma	7
Hydronephrosis (grade II or worse, Table VIII)	9
Pyelonephritis (Table VIII)	8
Hydronephrosis plus pyelonephritis (Table VIII)	4
Sensitivity of skin to ileostomy bag glue	1
Progressive bilateral hydronephrosis	5
Urinary calculus	2
8th nerve damage from streptomycin	2

*6 months or more after bladder substitution

TABLE V.—CLASSIFICATION OF ALL PREOPERATIVE AND POSTOPERATIVE PYELOGRAMS (130 RENAL UNITS, 65 PATIENTS)

	Preoperative	2 wks.	6 mos.	12 mos.	18 mos.	24 mos.	30 mos.	36 mos.
Normal	98	40	68	49	32	20	3	1
Grade I	4	19	29	20	10	6	1	1
Grade II	8	44	19	9	6	1		
Grade III	6	22	11	4	1	1		
Grade IV	14	5	3	2	1			
Total	130	130	130	84	50	28	4	2
No. patients	65	65	65	42	25	14	2	1

These patients have been classified as unsatisfactory because of grade II hydronephrosis or worse, regardless of their preoperative pyelographic status.

Pyelonephritis, with or without hydronephrosis, (12 patients), has been a troublesome problem only in those patients developing debility and cachexia from recurrent carcinoma. The remainder have had an occasional bout of fever and flank pain easily controlled by antibiotics or chemotherapy. Thus far, none have died of pyelonephritis or hydronephrosis as a late complication. (Patient M.M. is an exception who expired when reoperated upon because of urinary complications 2 months postoperatively, Table XV.)

Eleven of the 19 patients dying after the 6 months' follow-up period, had been classified as satisfactory. Ten of the 11 died of proved recurrent carcinoma; none are known to have died of urinary complications. The cause of death in 1 is unknown. Eight of the 19 patients had unsatisfactory ileal bladders for one or both of the two reasons. Seven patients died of recurrent carcinoma. The cause of death in 1 is unknown. Four of the 7 patients had definite pyelonephritis as part of the terminal picture.

TABLE VI.—CLASSIFICATION OF ALL PREOPERATIVE, 2 WEEKS, 6 MONTHS, AND LAST POSTOPERATIVE PYELOGRAMS (130 RENAL UNITS, 65 PATIENTS)

	Preoperative	2 wks.	6 mos.	Last IVP 6-36 mos.
Normal	98	40	68	85
Grade I	4	19	29	27
Grade II	8	44	19	6
Grade III	6	22	11	7
Grade IV	14	5	3	5

CLASSIFICATION OF PYELOGRAPHIC FINDINGS AFTER BLADDER SUBSTITUTION

In Tables V, VI, and VII, and IX to XV the intravenous pyelograms obtained on the 65 patients operated upon after 6 months or longer are classified according to the criteria set up. The pyelograms are tabulated as individual renal units. One renal unit, omitted from a previous report (3) because of the development of carcinoma of the kidney during the postoperative course, has been listed as normal in these tabulations because there was no hydronephrosis and no distortion before the development of renal carcinoma 6 months after bladder substitution. This accounts for the fact that the previous report contained an odd number of renal units while the present report contains an even number. Table V is the tabulation of all pyelograms available over the entire follow-up period. From this table it can be seen that 25 patients have been followed for 18 months or longer and that 42 of the 50 renal units in this group are satisfactory in that they are classified as normal or grade I. In order to add to the clarity of this table, pyelographic records were interpolated in a few instances in which 6 month periods had elapsed without the usual follow-up pyelographic studies. For instance, if the 6 and 18 month pyelograms were bilaterally normal, they were recorded as being normal at 12 months also. Similarly, if a renal unit was found to be grade III at 6 months and the next pyelograms at 24 months revealed it to be normal, the 12 and 18 month pyelograms are recorded on this table as grade II and grade I respectively. These interpolations were limited to a few intervening pyelograms and do not affect the end result recorded.

It is of interest to note (Table V) that of the 6 month postoperative pyelograms, 97 or 75 per cent of the 130 renal units are in the satisfactory category of normal or grade I. At 18 months, 42 of the 50 renal units followed for this period of time are satisfactory, ap-

proximately 84 per cent. The improvement in the postoperative pyelograms is quite apparent in this table; the grade II, III, and IV pyelograms decreased 50 per cent in number between 2 weeks and 6 months following operation. The transitory nature of the hydronephrosis occurring postoperatively is borne out by the graphs of the pyelographic data (chart 1), from which the following conclusions may be drawn: (1) The percentage of normal pyelograms 30 months postoperatively is the same as was present in the preoperative pyelograms. (2) The percentage of grade I pyelograms is significantly greater at all times after operation than before. (3) The percentage of unsatisfactory pyelograms (grades II to IV) is significantly less, 24 or more months after than before operation. Figures 1 and 2 show serial pyelograms illustrating the improvement of hydronephrosis which preceded (Fig. 2) and followed (Fig. 1) ureteroileal anastomosis.

Table VI indicates the results as determined by the last pyelographic studies on all of the 65 patients followed for 6 months or more. Examination of the final pyelograms varying from 6 to 36 months postoperatively reveals that 112 of the 130 renal units have been classified as normal or grade I. This indicates an 86 per cent satisfactory result as determined by interpretation of the pyelographic shadows.

Table VII corresponds to Table VI, but lists only the pyelograms on those patients now living. It can be seen from this table that there is no notable difference from the results recorded in Table VI which includes pyelograms of 19 patients who expired after the 6 months' follow-up period. Of the 92 renal units studied on living patients, 80 or roughly 87 per cent are satisfactory 6 to 36 months postoperatively.

Table IX shows the results of transplantation of 98 normal ureters. Approximately 50 per cent of all normal ureters transplanted show appreciable degrees of hydronephrosis when the 2 weeks postoperative pyelograms are made. The rapid improvement in the postoperative renal shadows is apparent in the 6 months pyelograms which then show 80 per cent to be in the satisfactory category. The

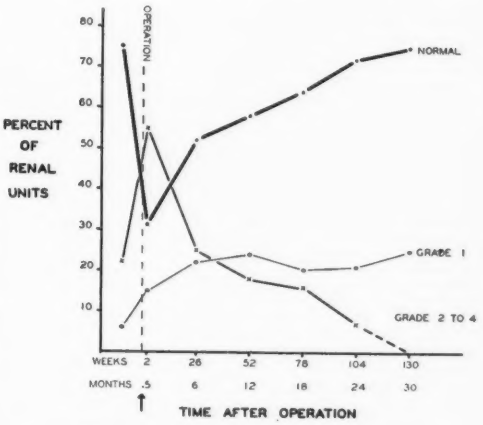

Chart 1. Graphs of pyelographic data.

subsequent gradual improvement in hydronephrotic pyelograms is evident in this table as well as in Table V. Only 1 of the 98 normal preoperative renal units became nonfunctional after transplantation.

The results of transplanting the hydronephrotic ureters are shown in Table X. Of the 28 hydronephrotic ureters, 6 were classified as normal or grade I at 2 weeks and this number has increased to 18 by the end of 6 months. During the same period the 14 renal units classified as showing no function on preoperative pyelograms were reduced to 2.

Table XI shows the fate of 2 weeks postoperative normal or grade I renal units. It will be seen that the 59 renal units so classified from the 2 weeks postoperative pyelograms remained essentially the same. On the other

TABLE VII.—CLASSIFICATION OF PREOPERATIVE, THE 2 WEEKS, 6 MONTHS AND LAST POSTOPERATIVE PYELOGRAMS ON PRESENTLY LIVING PATIENTS (92 RENAL UNITS, 46 PATIENTS)

	Preoperative	2 wks.	6 mos.	6-36 mos.
Normal	72	27	45	58
Grade I	3	8	22	22
Grade II	4	33	15	5
Grade III	4	20	9	5
Grade IV	9	4	1	2

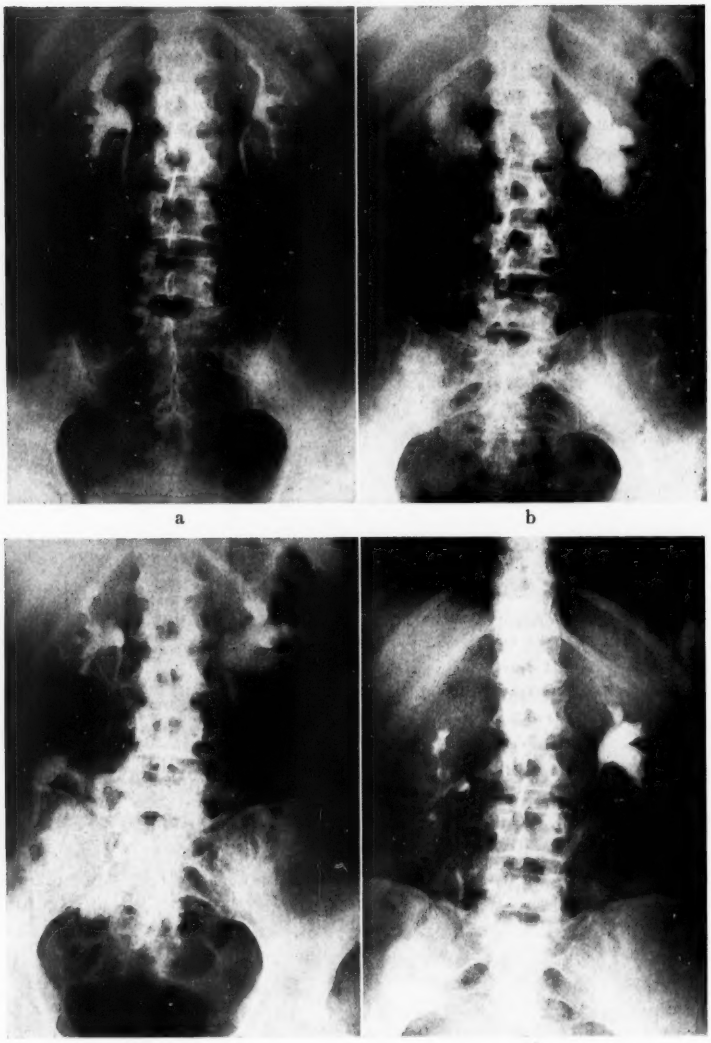

Fig. 1. Patient B.C. Pelvic exenteration for recurrent carcinoma of cervix after irradiation. a, Preoperative pyelogram, November 9, 1951, bilateral normal. Subsequent pyelograms show early postoperative hydronephrosis followed by rapid recovery. b, December 17, 1951, bilateral grade II hydronephrosis. c, January 16, 1952, right grade I, left grade II. d, November 11, 1952, right normal, left grade I. This patient did not have pyelonephritis.

hand, Table XII illustrates the fate of the 2 weeks postoperative hydronephrotic pyelograms, and it can be seen that there is a remarkable improvement in subsequent months. Over half (40) of the 71 renal units classified as grade II, III, or IV in the early postoperative films had advanced to normal or grade I by the end of 6 months. The relative percentage of normal and grade I renal units increases steadily over the subsequent follow-up period.

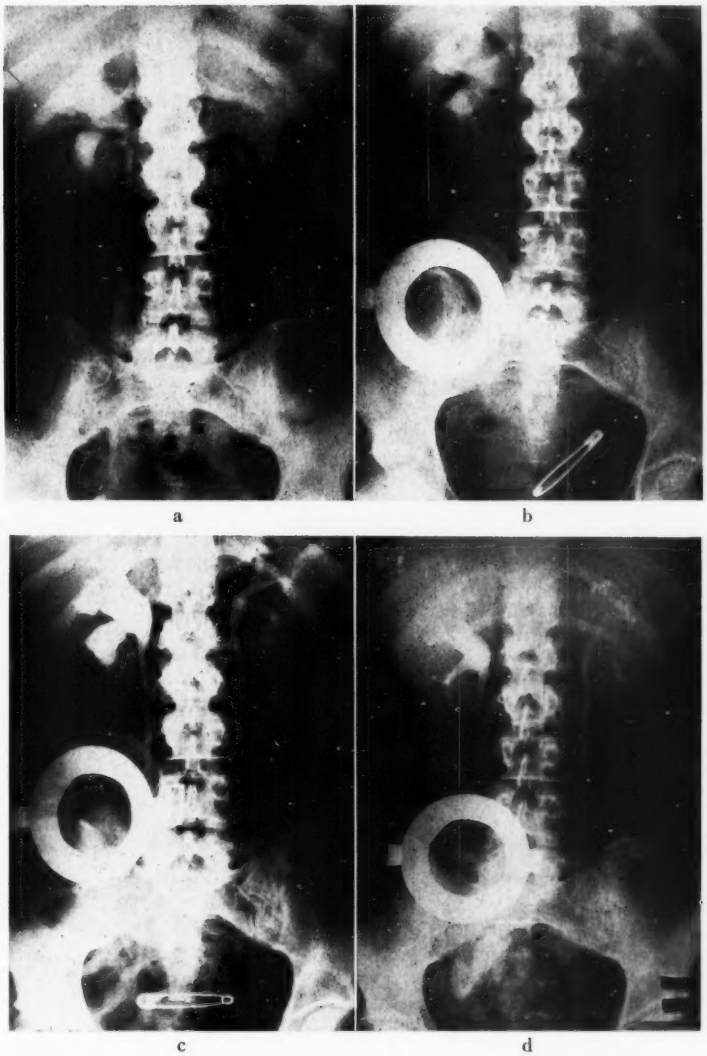

Fig. 2. Patient B.Y. Pelvic exenteration for recurrent carcinoma of cervix after irradiation. a, Preoperative pyelogram, February 9, 1953, right grade III, left grade IV. b, February 25, 1953, right grade III, left grade IV. c, March 14, 1953, right grade II, left grade I or normal (indicating lack of function on left preoperatively as being due to acute obstruction). d, March 20, 1953, right grade I, left normal. This patient did not have pyelonephritis.

Tables XIII and XIV show in detail the pyelographic studies on patients classified as unsatisfactory because of hydronephrosis or infection. It is of interest that there appears to be no correlation between the incidence of hydronephrosis and the occurrence of pyelonephritis. Nine patients had hydronephrosis without infection; 8 patients have had pyelonephritis without hydronephrosis; and, only 4 patients have had pyelonephritis in the

TABLE VIII.—CLASSIFICATION OF LATE RESULTS OF BLADDER SUBSTITUTION

	No. of cases	Per cent
65 patients available for study of late complications		
Satisfactory (5 patients had early infection not repeated for 12 mos. or over)	45	70
Unsatisfactory	21*	30
Because of hydronephrosis without pyelonephritis	9	
Because of pyelonephritis without hydronephrosis (3 of these had hydronephrosis earlier in postoperative course)	8	
Because of hydronephrosis plus pyelonephritis (4 of 12 with pyelonephritis developed infection in terminal phase of recurrent carcinoma)	4	
46 living patients available for study of late complications		
Satisfactory (4 patients had early infection not repeated for 12 mos. or over)	34	72
Unsatisfactory	12	
Because of hydronephrosis without pyelonephritis	7	
Because of pyelonephritis without hydronephrosis (2 of these had hydronephrosis earlier in postoperative course)	4	
Because of hydronephrosis plus pyelonephritis	1	

*This figure (21) includes 1 patient who died of recurrence without 6 month follow-up pyelograms, but who was known to have pyelonephritis. The patient is not included in the 65 available for study of late results, but is included here because of known infection.

presence of hydronephrosis either in one or in both kidneys.

HYPERCHLOREMIA AND ACIDOSIS

The complications resulting from the absorption of urinary constituents from the bowel have been absent. In only 2 patients has an elevated serum chloride been found at any time after operation. In both cases, now asymptomatic, ileal bladder substitution was performed for severe hyperchloremic acidosis incident to previous ureterosigmoidostomy.

TYPES OF INFECTION

The cause of pyelonephritis has been predominantly organisms of the coliform group. These infections have responded promptly to the administration of antibiotics known to be effective against gram negative bacilli. There have been 3 instances in which troublesome recurrent infection due to Proteus vulgaris has been refractory to treatment with the available antibiotics and chemotherapeutic drugs. Two of these patients developed infection as part of the terminal picture of recurrent carcinoma. The third is living and her infection is at present controlled with achromycin.

PROGRESSIVE BILATERAL HYDRONEPHROSIS

Five of the 65 patients included in the study of late complications have presented a picture of progressive bilateral hydronephrosis which led to the fear that longevity would be determined by this complication of bladder substitution rather than by the primary condition or disease for which bladder substitution was done. The pyelographic studies on these patients are presented in Table XV. In 2 patients the picture was associated with marked symptoms of pyelonephritis which led to early reoperation. One patient did not survive the revision procedure; the other procedure (G.H.) was successful, and the patient is now well with satisfactory pyelograms and with no evidence of pyelonephritis (18 months). Pyelograms of this patient are shown in Figure 3.

TABLE IX.—CLASSIFICATION OF PYELOGRAPHIC RESULTS OF TRANSPLANTATION OF NORMAL URETERS (98 RENAL UNITS FOLLOWED A MINIMUM OF 6 MONTHS)

	Pre-operative	2 wks.	6 mos.	12 mos.	18 mos.	24 mos.	30 mos.	36 mos.
Normal	98	36	56	44	28	19	3	1
Grade I		16	22	15	10	1	1	1
Grade II		34	14	6	2			
Grade III		11	5					
Grade IV		1	1	1				

TABLE X.—CLASSIFICATION OF PYELOGRAPHIC RESULTS OF TRANSPLANTATION OF HYDRONEPHROTIC URETERS (28 RENAL UNITS FOLLOWED A MINIMUM OF 6 MONTHS)

	Pre-operative	2 wks.	6 mos.	12 mos.	18 mos.	24 mos.	30 mos.
Normal		4	12	6	3	3	
Grade I		2	6	3	1	2	
Grade II	8	9	3	1	2	1	
Grade III	6	9	5	4	1	1	
Grade IV	14	4	2	1	1		

TABLE XI.—FATE OF 2 WEEKS POSTOPERATIVE NORMAL OR GRADE I RENAL UNITS AS DETERMINED BY SUBSEQUENT PYELOGRAMS

	2 wks.	6 mos.	12 mos.	18 mos.	24 mos.	30 mos.	36 mos.
Normal	40	50	33	15	8		
Grade I	19	7	4	4	1		
Grade II			3				
Grade III		2					
Grade IV							

TABLE XII.—FATE OF 2 WEEKS POSTOPERATIVE HYDRONEPHROSIS AS DETERMINED BY SUBSEQUENT PYELOGRAMS

	2 wks.	6 mos.	12 mos.	18 mos.	24 mos.	30 mos.	36 mos.
Normal		18	16	17	12	3	1
Grade I		22	16	6	5	1	1
Grade II	44	19	6	6	1		
Grade III	22	9	4	1	1		
Grade IV	5	3	2	1			

Two patients present the picture of progressive bilateral hydronephrosis, but have had no symptoms of infection; these patients are being closely observed. A fifth patient has expired from recurrent carcinoma after having developed bilateral hydronephrosis and uremia as a result of neglected stenosis of the ileostomy stoma. Since the complication of progressive bilateral hydronephrosis is of such major importance, the following brief case records of these patients are presented.

CASE 1. Patient M.M., a 51 year old white female upon whom a pelvic evisceration had been performed for an unclassified anaplastic tumor of the cervix. The preoperative intravenous pyelograms were normal. Two weeks postoperatively bilateral hydronephrosis of grade III severity was revealed. Six weeks postoperatively this patient was readmitted to the hospital for revision of the bladder substitution because of an increase in the degree of renal, pelvic, and ureteral dilation and because of repeated episodes of chills and fever. Soon after revision of the bladder substitute, the patient developed a fecal fistula which was undoubtedly secondary to mobilization of the small intestine from the pelvis and subsequent partial intestinal obstruction. During the patient's subsequent course, 3 laparotomies were done to re-establish the continuity of the intestinal tract without success. The patient died 4 months after pelvic evisceration and bladder substitution.

CASE 2. Patient G.H. (Fig. 3), a 52 year old white female, was subjected to pelvic evisceration for postsurgical, postirradiation recurrent endometrial carcinoma. Prior to operation intravenous pyelograms revealed normal renal shadows. However, multiple pyelograms taken after operation revealed the development of bilateral progressive hydronephrosis which was associated with repeated episodes of chills, fever, and costovertebral angle tenderness. Three and a half months postoperatively a revision of the bladder substitute was performed. Prior to this operation the renal status was classified as bilateral grade III hydronephrosis. Following the operation the pyelographic shadows reverted to normal on one side and grade I on the other. This patient has remained well since the ileal bladder revision and has had no further episodes of chills and fever (18 months).

CASE 3. Patient B.H., female, was subjected to exenteration of the pelvic viscera for postirradiation

TABLE XIII.—PYELOGRAPHIC STUDIES ON PATIENTS CLASSIFIED AS UNSATISFACTORY BECAUSE OF HYDRONEPHROSIS

Patient	Preop.		2 wks.		6 mos.		12 mos.		18 mos.		24 mos.		Remarks
	R	L	R	L	R	L	R	L	R	L	R	L	
H.W.	3	4	3	4	3	3	3	3	2	3	2	3	Well without symptoms
M.C.	0	0	3	3	0	2	0	2					Well without symptoms
A.Mc	0	0	1	2	1	2							Well without symptoms
M.L.	0	2	2	4	1	2							Well without symptoms
L.P.	1	4	3	3	3	3							Well without symptoms
P.V.	3	4	3	3	3	3	3	3					Well without symptoms
B.H.	0	0	1	1	3	3							Dead of recurrent ca.
I.M.	0	0	2	2	0	4							Dead of recurrent ca.
L.L.P.	0	0	2	2	3	3	2	4					No symptoms referable to G U tract

5 additional patients with hydronephrosis and infection listed in Table XIV

TABLE XIV.—PYELOGRAPHIC STUDIES ON PATIENTS CLASSIFIED AS UNSATISFACTORY BECAUSE OF PYELONEPHRITIS

Patient	Preop.		2 wks.		6 mos.		12 mos.		18 mos.		24 mos.		Remarks
	R	L	R	L	R	L	R	L	R	L	R	L	
V.S.	o	o	1	1	1	1	2	2	1	1	o	o	Dead of recurrent ca.
J.D.*	1	4	3	4	1	4							Dead of recurrent ca.
F.W.	o	o	o	1	o	o	o	o					Dead of recurrent ca.
R.A.S.*	4	4	o	o	o	o	1	2					Dead of recurrent ca.
A.L.*	o	4	o	2	o	2							Dead of recurrent ca.
H.N.	o	o	2	2	o	o							Dead of recurrent ca.
M.M.*	o	o	3	3									Died after reoperation at 2 mos.
G.H.*	o	o	2	2	o	1	o	1	o	1			Well after reoperation at 4 mos.
A.S.	1	4	3	3	2	2	2	2	2	2	1	1	Well except for mild episodes of infection
T.A.	o	o	o	o	o	o	o	o					Well except for mild episodes of infection
H.P.	o	o	2	2	2	2	1	1					Well except for mild episodes of infection
R.B.	2	4	1	2	o	o	o	1	o	1	o	1	Well except for mild episodes of infection
M.R.	1	4	(No postoperative pyelograms. Palliative operation. Died of cancer at 8 months, definite pyelonephritis before death)										

*Includes 5 patients with pyelonephritis plus hydronephrosis
Patient G.H. is listed as a satisfactory result in Table VIII since she has satisfactory pyelograms and has been without infection since revision of the bladder substitution over 2 years ago.

recurrent epidermoid carcinoma of the cervix. The postoperative course was uneventful until 4 months later when she was readmitted to the hospital in a semicomatose state from uremia. The ileostomy stoma was found to be stenosed and when dilated 500 cubic centimeters of dark foul smelling urine escaped. The stoma was revised to provide adequate drainage, and blood urea nitrogen subsided to a normal level. Intravenous pyelograms soon after admission revealed grade III hydronephrosis bilaterally which was thought to be due to stenosis of the ileostomy. The patient developed signs of recurrent carcinoma and the subsequent course was downhill until death 6 months after exenteration and bladder substitution.

CASE 4. Patient L.P., a 38 year old white female, had been subjected to pelvic evisceration for post-irradiation recurrent carcinoma of the cervix. The initial pyelograms revealed a normal renal shadow on the right and no evidence of function on the left. Two weeks postoperatively the pyelograms revealed grade III hydronephrosis on both sides. She has continued to maintain this degree of ureteropelvic dilatation, but has been entirely asymptomatic to date (8 months). If her benign clinical course should become complicated by either evidence of progression of hydronephrosis or by the onset of pyelonephritis, revision of the ureteroileostomies will be indicated.

CASE 5. Patient L.L.P. (Fig. 4), a 49 year old white female was subjected to pelvic evisceration

TABLE XV.—PYELOGRAPHIC STUDIES ON 5 PATIENTS HAVING BILATERAL PROGRESSIVE HYDRONEPHROSIS

Patient	Preop.		2 wks.		1 mo.		2 mos.		3 mos.		4 mos.		5 mos.		6 mos.		12 mos.		18 mos.		Remarks
	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L	
M.M.	o	o	3	3	3	3															Bladder revision fatal at 2 mos.
G.H.	o	o	2	2	2	2	3	3	3	3			1	o	1	o	1	o	1	o	Well since bladder revision at 4 mos.
B.H.	o	o	1	1							3	3									Died rec. ca. 6 mos. postop.
L.P.	1	4	3	3	3	3	3	3	3	3					3	3					Well and without symptoms
L.L.P.	o	o	2	2	3	3											4	2			No symptoms referable to GU tract

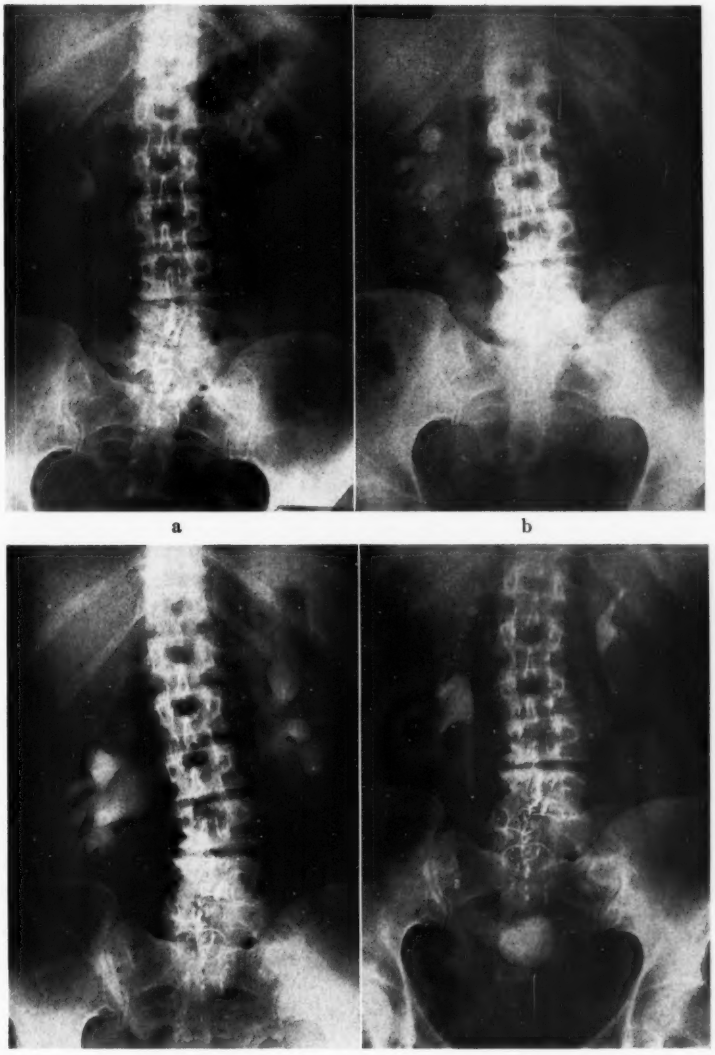

Fig. 3. Patient G.H. Pelvic exenteration for recurrent carcinoma of cervix after irradiation. a, Preoperative pyelogram, June 1, 1951, bilateral normal. b, June 22, 1951, right grade III, left grade IV. c, September 11, 1951, bilateral grade III with evidence of rapidly decreasing renal function and repeated chills and fever. Revision of ileal segment and anastomoses performed on September 13, 1951. d, January 21, 1952, right grade I, left normal. No recurrence of infection after revision.

for postsurgical, postirradiation recurrent adenocarcinoma of the cervix. Preoperatively intravenous pyelograms revealed normal renal units. Postoperatively the pyelograms revealed progressive hydronephrosis to grade III bilaterally with later change to grade II on the left and grade IV on the right. The most recent pyelographic studies indicate some improvement on one side, and since the patient is presenting symptoms of recurrent carcinoma, revision of the ureteroileostomies has been delayed.

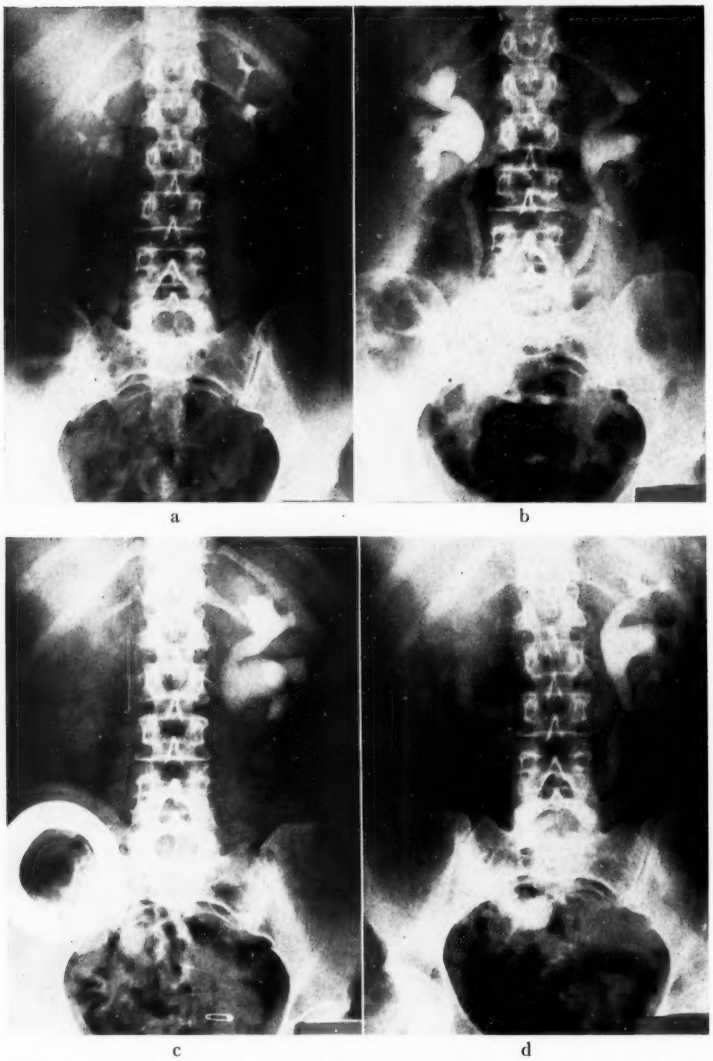

Fig. 4. Patient L.L.P. Pelvic exenteration for recurrent carcinoma of cervix after irradiation. a, Preoperative pyelogram, June 9, 1952, bilateral normal. b, July 2, 1952, bilateral grade III. c, February 18, 1953, right grade III or IV, left grade III. d, August 17, 1953, right grade IV, left grade II. This patient has had no clinical evidence of urinary infection. Since the left kidney is retaining function, and since her survival time is expected to be limited by the primary lesion, nothing will be done to alter this poor result of bladder substitution.

DISCUSSION

From the experience gained thus far with ileal segments as bladder substitutes, it appears that the results, as determined by pyelographic studies and the incidence of pyelonephritis, are superior to those that have been reported following ureterosigmoidostomy. The evaluation of an operation of this kind is

complicated and difficult to disassociate from the effects of the associated malignant disease which was present in the majority of the patients reported. However, in spite of this factor, ileal segment bladder substitution appears to have demonstrated certain advantages that make its continued trial and evaluation mandatory.

A discussion of the favorable aspects of this operation can be broken down into three parts: (1) the favorable results as determined by pyelographic studies, (2) the low incidence of postoperative pyelonephritis, and (3) the absence of hyperchloremia and acidosis as a complication of the operation.

It is our belief that the high percentage of satisfactory ureterointestinal anastomoses is due to the technique of the anastomosis itself and the fact that the ureter is anastomosed to a segment of bowel which is relatively clean and is isolated from the fecal stream. The dissection of the ureter and the method of anastomosis are aimed at the promotion of primary healing with a minimum of scar tissue reaction, and with as little of ureter as possible passing through as little of the bowel wall as possible. No attempt is made to prevent reflux by fashioning a valve or by tunneling the ureter. The absence of continued fecal contamination must have some favorable effect on rapid primary healing and on the continued satisfactory function of the anastomosis without obstruction, since subsequent inflammatory episodes leading to edema and fibrosis are minimized.

The low incidence of pyelonephritis appears to result from the satisfactory ureterointestinal anastomoses and the resultant low incidence of obstruction which produces stasis in the ureter and kidney pelvis. The incidence of infection is undoubtedly affected to some extent by the absence of the fecal stream, even though the urine in the ileal segment never becomes bacteria free. Another factor considered important is the lack of stagnation of urine in the bowel segments, since peristaltic action keeps them virtually empty (5). The absence of external obstruction in the form of a sphincter mechanism may militate against an increase in intraluminal pressure and thus decrease the chance of regurgitation of urine from the segment back into the ureters and kidney.

The absence of complications referable to absorption of chloride from the intestinal segments appears to be due to the small amount of intestinal mucosa that is in contact with the urine and to the rapid emptying of the segments. Absorption of urinary constituents by the intestinal segments is known to take place (4), but it has never led to the development of symptoms, nor has it been evident in blood chemical studies. Lapides believes that hyperchloremia and acidosis are the result of absorption of chloride plus diminished renal function. If his concept is correct, it is possible that the balance of these two factors might result in the characteristic chemical imbalance in a patient with an ileal segment substitute, but thus far we have not encountered it.

Although of secondary importance, the satisfaction of the patient with this method of disposing of the urine has been most gratifying in that it has so greatly simplified the follow-up care of the patient.

We now favor bladder substitution by this method as a means of decompressing bilaterally obstructed ureters (if the patient cannot be expected to have a return to normal bladder function in the future). In patients who may subsequently be subjected to bladder resection or pelvic exenteration, the abdominal operation for transplantation of the ureters affords an excellent chance to determine the operability of the primary lesion at the time the obstructed ureters are transplanted. The transplanting of hydronephrotic ureters is a safe procedure regardless of the degree of hydronephrosis or the presence of previous infection. There appears to be no more danger of developing pyelonephritis in a hydronephrotic kidney after ureterointestinal anastomosis by this method than in the normal kidney.

SUMMARY

The results of 106 bladder substitution procedures consisting of transplantation of both ureters to isolated segments of terminal ileum have been presented. The primary operation was pelvic evisceration in 81 patients and cystectomy in 16. Eight others had the procedure for palliation and 1 for neurogenic

incontinence. Sixty-five patients in this series have been followed from 6 to 36 months since operation by means of repeated intravenous pyelograms. There were 15 deaths in the 106 patients, 5 of which were thought definitely to be attributable to the bladder substitution procedure. The cause of death and the early and late complications have been presented in detail. Of the late complications those of hydronephrosis and pyelonephritis are considered to be of most significance because of their ultimate effect upon the longevity of the patient. Seventy per cent of the 65 patients reported are considered to have satisfactory results in that the pyelographic shadows of both kidneys are satisfactory and they are free of clinical evidence of pyelonephritis. Thirty per cent of the 65 patients are unsatisfactory in that they have either unsatisfactory pyelograms or clinical evidence of pyelonephritis, or both. Eighty-six per cent of the 130 renal units involved in the 65 bladder substitution procedures were either normal or showed a minimal degree of hydronephrosis 6 to 36 months after operation. None of the patients have developed hyperchloremic acidosis.

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PULMONARY ADENOMATOSIS

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PULMONARY adenomatosis[1] in terms of medical interest can be called a very new disease. Recently, the point of view is becoming accepted that this entity is, in actuality, a variant of bronchiolar carcinoma, possessing a relatively low grade of malignancy. During the 75 year period from 1876, when the first case was reported by Malassez, until 1945, only 25 cases were described. In the past 8 years, however, over 7 times this number of cases have been reported. This sudden increase does not necessarily indicate that pulmonary adenomatosis is becoming more common. Instead, until more evidence is available, it must be assumed that the increase can be attributed to more frequent recognition of the condition, which, in turn, results from the heightened interest in pulmonary neoplasms in recent years. In any event, it may be expected that these tumors will be reported with greater frequency in the future and that a substantial percentage of all new cases of pulmonary growths show the histologic pattern of pulmonary adenomatosis.

The purpose of this report is to add 4 new cases to the total of 217 described to date. These cases are of particular interest, we think, because of the cytologic procedures used in their study. In addition, we have included a brief re-evaluation on the basis of further cytologic studies of a case reported by Stephens and Shipman 5 years ago.

We have approached the problem of cytologic diagnosis of adenomatosis by attempting to correlate cytologic findings with results of other morphologic studies. For this purpose, we found that sections of lung tissue stained by the Papanicolaou method (7, 8) provided an accurate basis for cytologic comparison and proved of great value in aiding definition of the peculiar morphologic features of this disease.

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[1]Also known as: Bronchiolar carcinoma; papillary gelatinous adenocarcinoma; alveolar cell carcinoma; multicentric alveolar cell carcinoma; primary multiple alveolar cell tumor; carcinomatoides alveogenica multicentrica; multicellular papillary adenocarcinoma; diffuse primary alveolar epithelial carcinoma; malignant adenomatosis; carcinosis of the lungs; diffuse pulmonary epithelial hyperplasia; alveolar cell tumor; and adenoma-like tumor.

NOMENCLATURE

The variety of terms used to designate these tumors, as well as the diversity of opinions regarding their malignancy or benignancy and their etiology, reflect the uncertain knowledge of their histogenesis. Swan was the first to propose a set of morphologic criteria for their identification. He suggested reserving the term "pulmonary adenomatosis" for those cases distinguished by: (1) alveolar-cell proliferation, characterized by the appearance of additional mucus-producing cells; (2) absence of an intrinsic tumor of the bronchial tree; and (3) absence of primary carcinoma in other parts of the body. He also proposed that those adenomatoses which metastasize should be termed "cancerous adenomatoses."

Storey, Knudtson, and Lawrence, on the basis of an analysis of 205 of the 217 cases known to medical science (including 37 cases reported by them for the first time), qualified these criteria. They called attention to the fact that characteristically the tumor is composed of alveoli lined by columnar or cuboidal epithelial cells with eosinophilic cytoplasm and basally placed nuclei. They also commented on the typical preservation of the pulmonary architecture in this condition. These investigators, as well as Liebow and Steward (3), Watson and Smith, and numerous others, have concluded that these lesions are carcinomas of bronchiolar origin and reject the designation "pulmonary adenomatosis" as misleading.

The multiplicity of synonyms, while confusing, is not of primary importance, at least until the histogenesis of these tumors is determined. We have chosen to use the term

Fig. 1. Typical lung section—pulmonary adenomatosis ×209 showing abundant cellular material lying within the alveolar spaces.

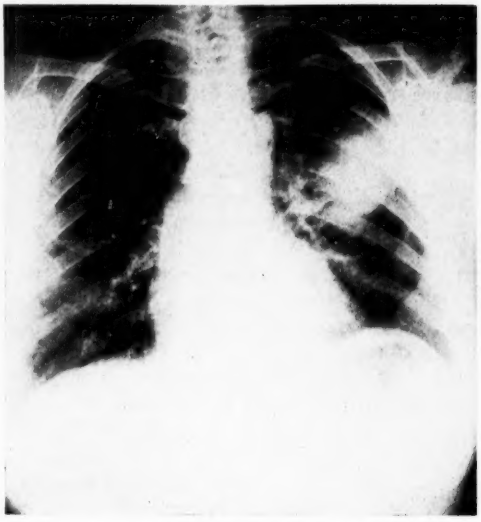

Fig. 2. Case 1. Posteroanterior film of chest showing a large dense, round infiltration in the left upper lobe of the lung.

"pulmonary adenomatosis" because it avoids the etiologic bias attached to more specific nomenclature. In so doing, it is not our intention to minimize any of the evidence supporting the view that this lesion is a neoplasm which could appropriately be called bronchiolar carcinoma.

PATHOGENESIS

According to Storey and his associates, metastases occur in over half of all cases of pulmonary adenomatosis. Upon cursory examination it might seem that certain classical characteristics of carcinoma are not exhibited by these tumors. Among these might be cited the preservation of pulmonary architecture, which is an outstanding feature of pulmonary adenomatosis.

Another variance from classical criteria has to do with the occasional long periods of apparent stabilization of the disease which have been noted in our own and in other cases. Neither of these points is critical or conclusive.

The obvious parallel between human adenomatosis and similar lesions in animals (sheep, guinea pigs, horses) is striking. Both diseases are characterized by multiple lesions consisting of tall ciliated and nonciliated columnar cells and high cuboidal epithelial-like cells which rarely contain mitotic figures. In both diseases there is a marked absence of stromal invasion. Although one might wish for more detailed studies of "jaagsiekte," the conviction of all observers that the disease is transmitted by the penning of healthy sheep with sick ones leads to the assumption that "jaagsiekte" is a communicable disease, and hence, by present standards, is not a neoplastic one. The fact that metastasis to lymph nodes has been reported to occur in "jaagsiekte," however, weakens this hypothesis.

According to our present knowledge, there is no reason to suppose that pulmonary adenomatosis is transmitted from one human being to another. This condition may well prove to be neoplastic in origin, but as long as so many questions remain unanswered, any conclusion as to the etiology of pulmonary adenomatosis seems premature.

PATHOLOGY

Grossly, the tumors are nodular or diffuse masses which lie in the peripheral areas of the lung. In appearance, they often resemble the

Fig. 3. Case 1. Cells seen in sputum. Note extensive vacuolization and tightness of grouping. ×471.

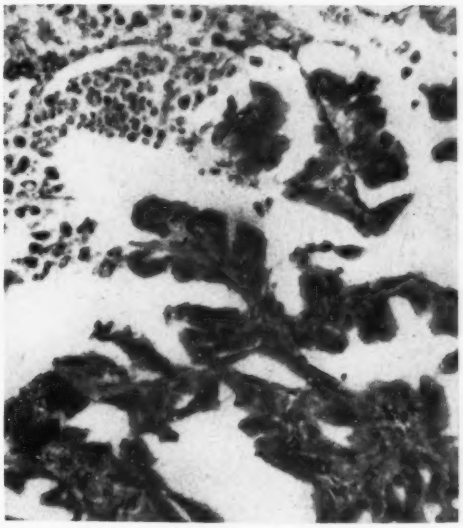

Fig. 4. Case 1. Lung section. Note papillary proliferation of alveolar architecture. ×471.

lesions of tuberculosis or pneumonia. The nodular and diffuse forms show no significant differences histologically and it is suggested that they represent different stages of the same disease. The larger and smaller bronchi are usually not involved by the new growth, but the bronchi which drain the affected areas may contain frothy, mucinous fluid. Postmortem examination often reveals adhesions between the lung and the chest wall and fluid in the pleural and pericardial cavities. Pneumonia is often the immediate cause of death.

Microscopically, this tumor is seen to consist of alveoli lined with columnar or cuboidal cells which often form papillae and project into the alveolar lumina. Occasionally, these cells are ciliated and in rare instances they are seen in mitosis. Exfoliated cells are often found grouped in the alveolar spaces (Fig. 1), and Hutchinson has suggested that the movement of these cell clusters within the lung accounts for the apparent multicentric character of adenomatoses.

The fact that the alveolar structure, bronchioli, and lung septi are often preserved to a considerable extent suggests that the destructive properties of the tumor are limited. These growths, however, render the lungs susceptible to pneumonia, which enhances the destruction of the lung parenchyma. Consequently, pathologic studies are sometimes complicated by the pronounced inflammatory processes in and around the growth and the frequent presence of abscesses. Metastatic spread may take place within the lung via the air passages, as suggested by Hutchison, and more widely by means of the lymph and blood channels. Storey, Knudtson, and Lawrence recently reported metastatic lesions in 54 per cent of their cases. In 35 per cent of these patients there was local spread only (mediastinal lymph nodes, pleura, pericardium, and diaphragm) and in 36 per cent both local and distant spread. In the remaining 29 per cent, there was distant spread only which, according to these authors, demonstrated the frequency of blood-borne metastases. It is of interest that metastatic lesions in the lung from adenocarcinomas elsewhere in the body, for example, from pseudomucinous cystadenocarcinoma of the ovary, may resemble adenomatosis microscopically.

CLINICAL ASPECT

Because of the increasing number of reported cases, the exact incidence of pulmonary

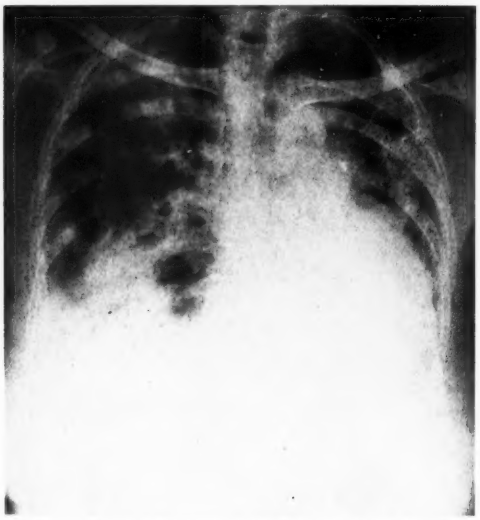

Fig. 5. Case 2. Posteroanterior film of chest showing a diffuse linear and nodular infiltration in right upper lobe and an almost homogeneous density of the left lower lobe.

Fig. 6. Case 2. Cells demonstrated in sputum which show extreme vacuolization of the cells with uniform nuclei. ×471.

adenomatosis is difficult to estimate. Also, it is probable that many of these tumors have been improperly classified as bronchogenic carcinoma. This assumption is supported by the work of Watson and Smith who found 33 incidences of pulmonary adenomatosis in a series of 1,585 reported cases of malignant lung lesions. According to Storey, approximately 5 per cent of all pulmonary carcinomas are actually adenomatosis. Although definite data are lacking, it is doubtful that racial predilection exists. A peculiarity of the disease is that, in contrast to bronchogenic carcinoma, it affects approximately as many women as men. The 4 patients presented in this study, who incidentally were all women, ranged in age from 54 to 70 years. The majority of patients are in the so-called cancer age group, although the disease has also been described in a boy only 16 years old and in an 89 year old man.

SYMPTOMS AND SIGNS

Most authors list dyspnea as the most common symptom of pulmonary adenomatosis. Cough, however, is far more frequent according to our experience and to that of Storey, who reported that 107 (50 per cent) of his 154 patients manifested this symptom. The cough characteristic of pulmonary adenomatosis is productive of mucoid sputum, which varies from watery to thick in consistency and which has been described as resembling soap suds or foam. The sputum is produced in unusually large amounts; many authors consider this peculiar bronchorrhea pathognomonic of pulmonary adenomatosis. Chest pain, usually mild in degree, apparently results from pleural involvement. None of these symptoms is sufficiently specific to permit diagnosis on clinical grounds alone. The condition is usually recognized only after surgical exploration of the chest or at postmortem examination. The physical signs are even less characteristic and vary according to the extent of the disease. The laboratory findings are generally noncontributory. Moderate to severe leucocytosis has been observed but seems to be related to secondary infections. Occasional elevations of the sedimentation rate have also been noted, especially in well established cases.

All of our 4 patients suffered from cough for periods varying from 1 to 24 months. In 2 of the patients the sputum was occasionally blood-streaked, but no instance of frank hemoptysis was observed. Although loss of

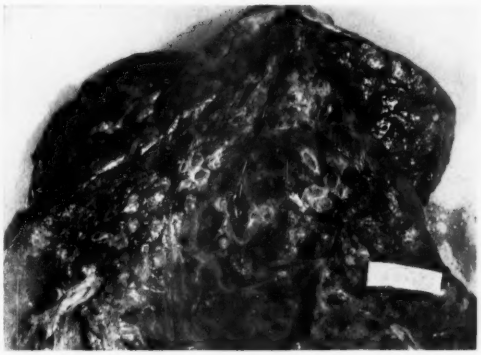

Fig. 7.

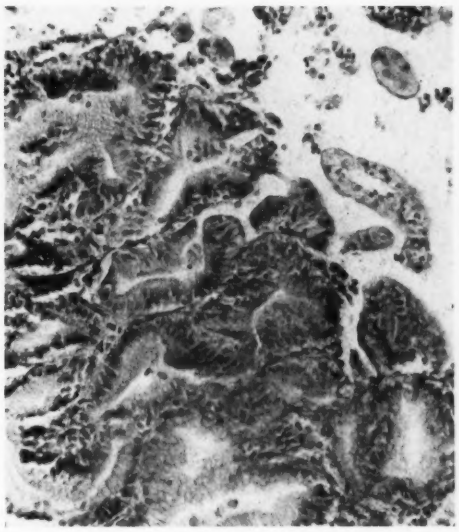

Fig. 8.

Fig. 7. Case 2. Gross section of left lung obtained at autopsy showing intact bronchial lumina and numerous whitish gray nodules and diffuse areas of tumor infiltration.
Fig. 8. Case 2. Lung section showing alveolar-like pattern and lining of tall columnar epithelium. ×471.

weight is usual in this condition, 1 of our patients in whom the disease was well established gained 25 pounds.

ROENTGENOGRAPHIC ASPECTS

The roentgenographic aspects of pulmonary adenomatosis are as variable and atypical as the clinical manifestations. Lesions ranging from a solitary unilateral nodule to multiple bilateral nodules and varying widely in size and shape have been described. The ideal, resectable, solitary, peripheral nodule has been found in only one-fourth of all reported cases. Serial x-ray films often show a homogeneous density due to coalescence of nodules, and the combination of a large lobar density and multiple nodules is not infrequent.

CYTOLOGIC ASPECTS

Numerous investigators, including Papanicolaou (6), MacDonald, and Watson, have reported upon the cytologic aspects of this disease and most of these authors have commented upon the abundance of diagnostic cells in the sputum. This profusion undoubtedly results from the pronounced tendency of this growth to shed characteristic cells into the draining passages of the bronchial tree. It seems likely that this exfoliation is even more profuse in adenomatosis than in typical carcinoma of the lung.

An analysis of the reported cytologic studies of cases of pulmonary adenomatosis reveals some rather encouraging findings. In the Storey series of 37 cases which had not previously been reported, only 35 per cent were studied cytologically; and of this number studied, 66 per cent were reported as negative, 20 per cent as group V (malignant), and 13 per cent as group III (inconclusive). A much more promising cytologic result is seen in his review of a larger series of previously reported cases. In this series of 120 cases collected from 1947 to 1953, only 26 per cent (32 cases) were studied cytologically; however, in this group, negative results were reported in only 19 per cent (6 cases). The remaining 81 per cent were given reports which indicated that further study was needed. Thirty-eight per cent (12 cases) were reported as group V (malignant cells present), 31 per cent were reported as group III (inconclusive), and in 12 per cent (4 cases), a specific reference to pulmonary adenomatosis (using this term or one of the many other designations for this disease) was included in the report.

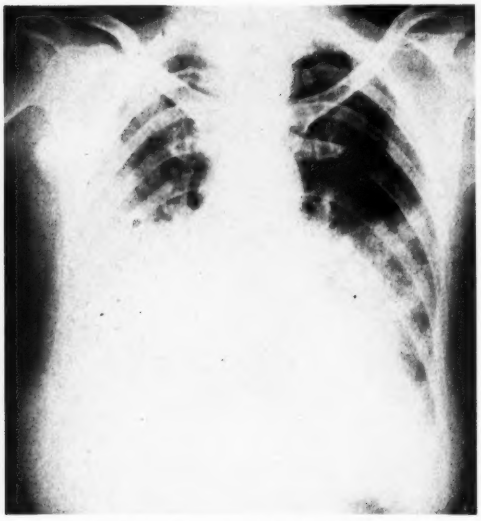

Fig. 9. Case 3. Posteroanterior film of chest showing homogeneous densities of both lower lung fields with linear and nodular densities in right upper lobe.

Fig. 10. Case 3. Cells in sputum which demonstrate distorted nuclei due to pressure of the vacuolization. ×471.

REPORT OF CASES

CASE 1. M.O., a 70 year old white female, who had been well previously, developed a cold which was associated with cough productive of increasing amounts of sputum in September 1948. Physical examination at that time revealed evidence of disease in the left upper lung field (Fig. 2). Results of laboratory examinations were essentially noncontributory, except that specimens of sputum studied cytologically were reported to contain malignant cells (group V) (Fig. 3). The patient went downhill very rapidly and died 5 months after the onset of symptoms. At autopsy, the lateral surface of the left upper lobe was found to be scarred, retracted, and darkish-red in color. A section through this area revealed a firm, diffuse grayish tumor. On gross examination, no evidence of tumor was seen in the trachea and bronchi, and the mediastinal lymph nodes showed no abnormalities. Microscopic study of sections from the tumor in the lung showed the alveolar walls to be lined by tall columnar and cuboidal cells (Fig. 4). Metastatic tumor cells in irregular groups and in fairly well defined acinar patterns were also found in one hilar lymph node. A diagnosis of alveolar-cell carcinoma was reported.

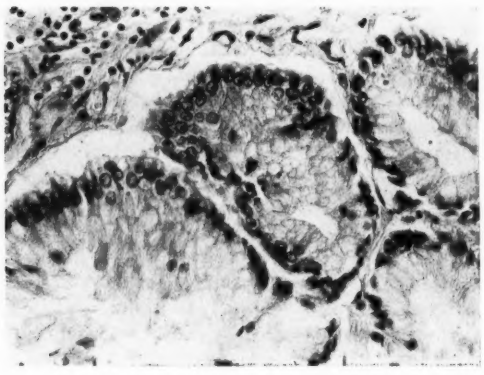

Fig. 11. Case 3. Section of lung showing alveoli-like structures lined by tall columnar epithelium. ×471.

CASE 2. I.A., a 56 year old white female housewife, was admitted to San Francisco Hospital in December 1950 because of cough productive of thin, whitish sputum, occasionally streaked with blood, of 6 months' duration. Clinical and laboratory examinations, including a bronchoscopy, were negative. On the basis of x-ray findings (Fig. 5), a left lower lobectomy was performed in January 1951 and a diagnosis of adenocarcinoma was made from lung sections.

Two years later, results of cytologic examination of sputum were reported as inconclusive (group III), but the diagnosis of pulmonary adenomatosis was suggested (Fig. 6). The surgical specimens were then re-examined and the diagnosis was changed to pulmonary adenomatosis. During the years following surgery, the patient continued to show x-ray evidence of active disease in the left lung. Cytologic examinations of the sputum consistently revealed cells suggestive of pulmonary adenomatosis. The disease process became progressive and bilateral, and the patient died 3 years after the onset of symptoms.

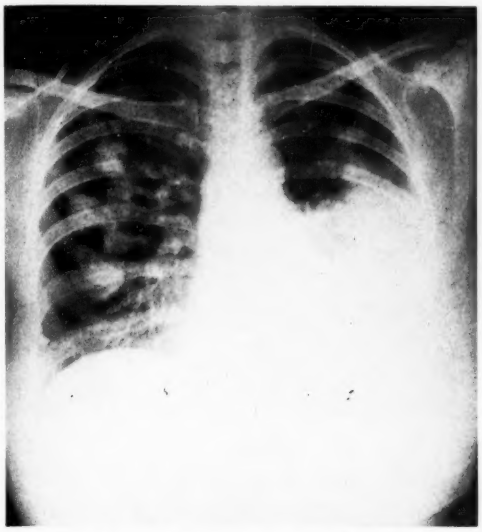

Fig. 12. Case 4. Posteroanterior chest film showing multiple, large, nodular densities throughout the right lobe and a large homogenous density over the left lower lobe.

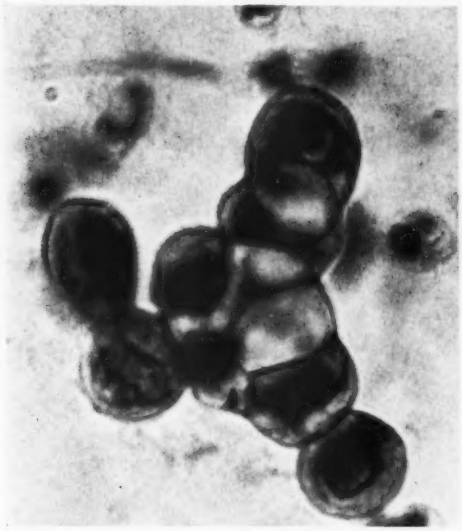

Fig. 13. Case 4. Cells seen in sputum. Note the similarity to the cells which are illustrated in preceding figures. ×471.

The gross appearance of the lung in this case is shown in Figure 7, and the changes in the lung tissue characteristic of this disease may be seen in Figure 8. Direct smears made at autopsy from the tumor areas and from the abundant frothy material aspirated from the bronchi revealed the same characteristic cellular morphology seen in tissue and sputum specimens.

CASE 3. M.C., a 67 year old housewife with a 2 year history of cough productive of several cupfuls of white or yellowish sputum which was occasionally streaked with blood, was admitted to the San Francisco Hospital in November 1950 (Fig. 9). Cytologic studies showed group V (malignant) cells in the sputum (Fig. 10). The patient declined slowly and died 7 months after hospitalization. Upon autopsy, which followed embalming, the involved portions of the lung showed a resemblance to lobar pneumonia in the stage of gray hepatization. No evidence of tumor was seen in the tracheobronchial tree and no evidence of metastasis was found. A diagnosis of pulmonary adenomatosis was made from histologic examination of the lung tissue (Fig. 11).

CASE 4. F.D., a 54 year old housewife, had been in good health until April 1950 when she developed a slight cold with a cough. Repeated colds and continued cough led to her admission to the University of California Hospital in November 1951, nineteen months after the onset of symptoms. Bronchoscopy showed no abnormality. Cytologic studies of sputum and bronchial washings showed group III (inconclusive) cells suggestive of pulmonary adenomatosis (Fig. 13). A lung biopsy performed in November 1951 confirmed this diagnosis. The patient died in May 1952; the postmortem diagnosis was pulmonary adenomatosis.

CASE 5. I.B. is a patient who had been definitely exposed to sick sheep. (This interesting case was reported in detail by Stephens and Shipman in 1949.) The opportunity to make further cytologic studies of the patient's sputum during the past year renewed our interest in the case. The patient's history of pulmonary symptoms dates back 14 years, and she was first admitted to the University of California Hospital in the Spring of 1948. In May of 1948, the right lower lung was removed and a pathologic diagnosis of pulmonary adenomatosis was made. Although the patient has remained alive, progressive involvement has been noted in both lungs. Recent sputum specimens examined in our pulmonary cytology laboratory contained cells reported as group III (inconclusive) and suggestive of pulmonary adenomatosis (Fig. 14).

SPUTUM CYTOLOGY AND ADENOMATOSIS—A SUMMARY OF FINDINGS

We have become increasingly interested in the potentialities of cytologic studies in cases of pulmonary adenomatosis since our first case (Case 1) 5 years ago. The sputum studies from this case as well as from Case 3 were reported as group V (malignant). The remaining 3 were reported as group III (inconclu-

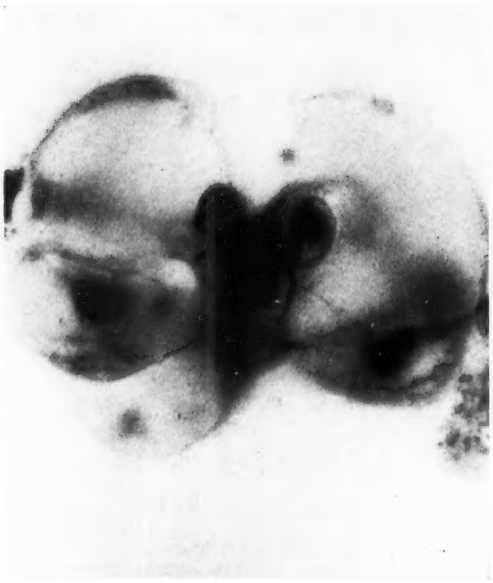

Fig. 14.

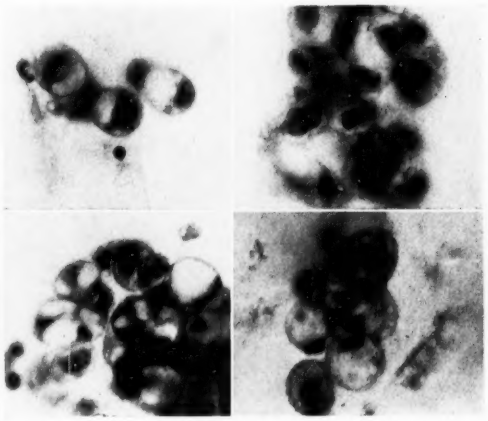

Fig. 15.

Fig. 14. Case 5. Cells in sputum. ×471.
Fig. 15. Typical cell groups seen in the sputum of patients with pulmonary adenomatosis. ×74.

sive), and the report contained a specific reference to pulmonary adenomatosis as possible diagnosis.

A review of the sputum smears from these cases disclosed a typical cytologic picture (Fig. 15). The grouping of the cells in all instances was consistent with malignancy. The presence of the numerous, large, compact groups of nonciliated acini was strongly suggestive of adenocarcinoma. Massive vacuolization (usually one large vacuole per cell) was frequently seen within the cytoplasm. The wide variation in nuclear size and shape characteristic of adenocarcinoma, however, was not a prominent feature. In general, only single, small nucleoli were seen. Apparently, the pressure of the enormous vacuoles tended to push the nuclei peripherally with resulting compression.

In brief, the grouping of the cells shed from the lesions of pulmonary adenomatosis showed a remarkable resemblance to the acini of adenocarcinoma, however, the appearance of the nuclei, which was not typical of cancer cells, was evidenced against a group V diagnosis of malignancy.

It seems appropriate to point out that the accuracy of present cytologic techniques has coincided with an increasing reliance upon nuclear criteria. For example, in the early application of cytologic methods to the diagnosis of lung cancer, false positive results were often reported in studies of the sputum of patients with asthma. In asthma, the sputum characteristically contains numerous mucus-producing columnar cells in tight, extensively vacuolated groups, which closely resemble the acini of adenocarcinoma. However, the nuclei of these cells are uniformly small and do not fulfill the criteria for cancer. Cilia are often seen about the periphery of such cell groups, and the presence of eosinophils and Curschmann's spirals offers further aid in differentiating this disease from carcinoma of the lung.

A parallel, then, does exist between the cells typical of asthma and the cells typical of pulmonary adenomatosis, in that they show a comparable difference from the cells characteristic of malignancy. We do not mean to state categorically that this parallel rules out the possibility that pulmonary adenomatosis is malignant in origin. We would call atten-

tion to the fact that all of our experience with cytology stresses the importance of nuclear criteria of malignancy. Nuclear appearances are important not only in differentiating carcinoma of the lung from asthma but also in eliminating other benign pulmonary conditions, such as lipid pneumonia, bronchial adenoma, bronchiectasis, and pulmonary infarction, as a source of false positive reports.

We also do not claim that cytologic study of the sputum will detect pulmonary adenomatosis with unfailing accuracy. We are convinced, however, that attention to nuclear appearances will frequently suggest the possibility of adenomatosis, which can then be confirmed or disproved by other diagnostic studies.

SUMMARY

1. A review of the nomenclature, etiology, pathology, symptomatology, roentgenographic and cytologic aspects of pulmonary adenomatosis is presented.

2. Four new cases are reported and discussed in relation to the clinical, cytologic, and pathologic findings.

3. A case, reported by Stephens and Shipman in 1949, is re-evaluated on the basis of further cytologic studies.

4. The value of sputum cytology in pulmonary adenomatosis is discussed and a summary of the findings presented.

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A COMPARATIVE STUDY OF THE METHODS FOR THE PREVENTION OF AMPUTATION NEUROMA

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THE prevention of amputation neuroma has been the subject of extensive studies, engaging the attention of surgeons, especially since the first World War. The fact that more than a score of methods have been and are being used is evidence that no method has proved entirely satisfactory.

There seems to be no unanimity of opinion regarding the treatment of nerves at the time of amputation, and the conflicting results available in the literature suggest that the problem remains unsolved. Bardenheuer, von Kruger, Corner, Laewen (18, 19), Hedri (12, 13), Huber and Lewis have suggested different methods for the prevention of neuroma formation. Beswerschenko used the technique proposed by von Kruger, Bardenheuer, and others. No entirely satisfactory method has been described as shown by the more recent studies of Guttmann and Medawar, Boldrey, Troitskiy, Herrmann and Gibbs, Edds, Jr., Finocchiaro, Padovani and Mansuy, Chenilleau, Kirk, Dogliotti, Teneff, and Micheli, Padovani, Teneff, Strahberger, and others concerning the problem of amputation neuroma and methods of its prevention. However, very few studies have been made on a comparative basis, and we felt that a study of the various methods used to prevent the formation of amputation neuroma would be of interest.

We present here the results obtained by the experimental study of different methods.

MATERIAL AND METHODS

Adult rats were used in our experiments and the following fundamental operation was performed.

One centimeter of the sciatic nerve was resected. The operation was made under ether anesthesia and asepsis. The nerves were sectioned with a sharp blade, and fine cotton thread (No. 50) was used in every case in which ligature was made. The following treatments were carried out:

Group A—38 animals. The sciatic nerve was exposed, dissected and sectioned, without further treatment. In all cases typical neuroma formation occurred.

Group B—13 animals. A ligature with cotton thread was made before resecting the nerve. Typical neuroma formation was present in every case.

Group C—10 animals. The nerve was ligated and a collodium cuff placed around the stump. Neuroma formation was observed in every case.

Group D—16 animals. After sectioning the nerve, a collodium cuff was placed around the stump. In 2 cases no neuroma was observed.

Group E—13 animals. The nerve was ligated and the stump injected with approximately 0.25 milliliter of aqueous 2 per cent gentian violet. In 10 instances the development of neuroma could be demonstrated.

Group F—17 animals. The nerve stump was ligated and an injection of approximately 0.25 milliliter of 10 per cent formaldehyde was made. Neuromas developed in 13 cases.

Group G—12 animals. The nerve was ligated and injected with absolute alcohol. In 10 instances typical neuroma formation occurred.

Group H—22 animals. The nerve was ligated and 0.25 milliliter of 2 per cent gentian violet injected. Tannic acid powder was placed around the stump and covered with a collodium cuff. In 11 cases no neuroma was observed.

Group I—13 animals. The nerve was placed unsutured between muscle fibers adjacent to the amputation site. In all in-

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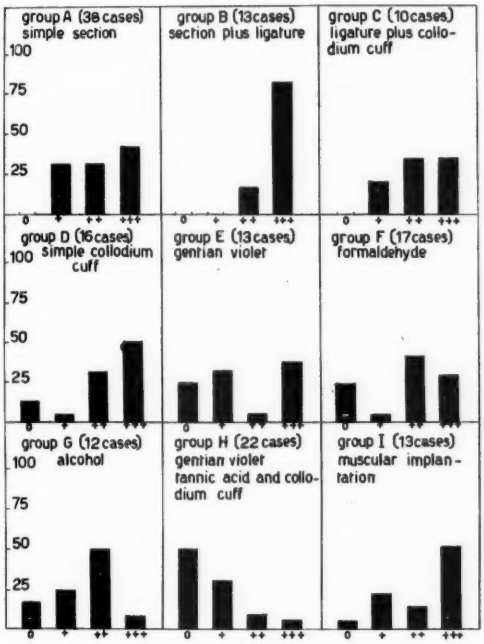
group A (38 cases) simple section
group B (13 cases) section plus ligature
group C (10 cases) ligature plus collodium cuff
group D (16 cases) simple collodium cuff
group E (13 cases) gentian violet
group F (17 cases) formaldehyde
group G (12 cases) alcohol
group H (22 cases) gentian violet tannic acid and collodium cuff
group I (13 cases) muscular implantation
100
75
50
25
0
+
++
+++

Fig. 1. Diagram of percentages on the incidence and density of neuroma formation in the different experimental groups. Density of neuroma formed, expressed in crosses according to the criteria explained in the text. In ordinate percentage of total cases.

stances except 1, typical neuroma formation occurred.

Previous experiments had demonstrated that amputation neuroma develops within a month after the section. In a period ranging from 50 to 378 days after nerve section, the animals were sacrificed, and specimens of the nerve submitted to microscopic study. Sections were made by using the pyridine method of Ranson as described by Conn and Darrow in order to study the neurofibrils. Specimens fixed in formalin solution and in Helly's fluid were stained with hematoxylin and eosin or Mallory's trichrome for complementary studies. Animals submitted to nerve section always presented paralysis of the limb, leading to the formation of callosities (Fig. 2).

RESULTS AND CONCLUSIONS

The density of the neuroma formed was evaluated by an arbitrary scale, according to the following criteria: +, slight neurofibrillar crossing (Fig. 3); ++, marked neurofibrillar crossing (Fig. 4); +++, formation of a terminal bulb with very marked nerve fibers crossing (Figs. 5 and 12).

The slides were studied at two different periods with very close agreement of the results.

Figure 1 illustrates the results obtained, showing the different degrees of density of the neuroma formation verified after each treatment. Observation of Figure 1 shows that when the nerve is sectioned without further treatment, with a simple ligature, or with a ligature protected by a collodium cuff, a typical neuroma of densities ++ and +++ is formed in at least two-thirds of the cases. These results agree with those found by Poth, Bravo-Fernandez, and Drager (24) who obtained a typical neuroma in cases of simple nerve section. Simple ligature after nerve section not only does not prevent but actually seems to promote neuroma formation, as judged by the density of neurofibrillar crossing (Figs. 5 and 6). Simple ligature does not prevent neurofibrillar growth, for in almost all cases one can observe fibrils over the ligature forming irregular bundles of fibers that contribute to the neuroma formation (Figs. 6, 7, and 8).

The changes observed by Weiss and Hiscoe due to acute constriction ("damming effect") and described as irregularities of the neurofibrils located above the constriction zone were present in our material (Figs. 9 and 10).

Fig. 2. Callosities formed in the legs of rats with sectioned sciatic nerve.

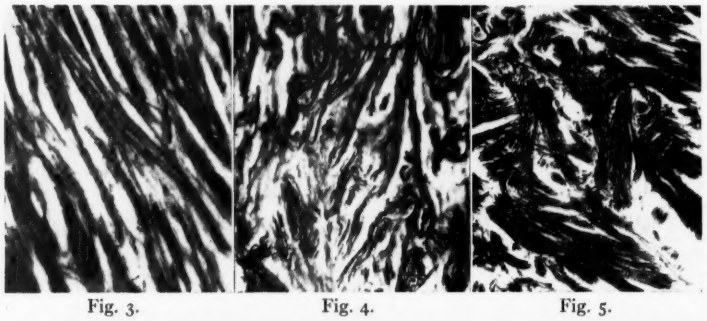

Fig. 3. Fig. 4. Fig. 5.

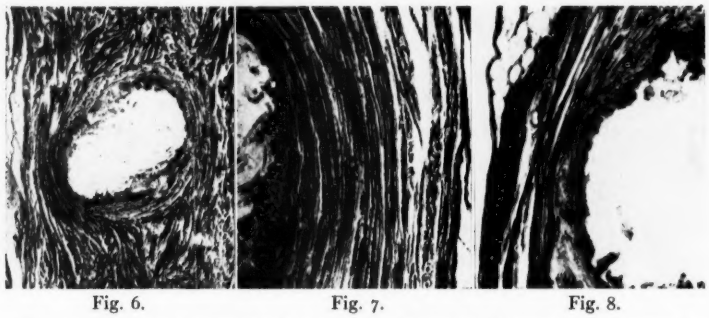

Fig. 6. Fig. 7. Fig. 8.

Fig. 3. Section[1] of a nerve 262 days after simple section. Observe little intercrossing of neurofibrils. This case was considered as grade +. × 179.

Fig. 4. Nerve 206 days after simple section (Group A). Grade ++ with moderate neurofibril intercrossing. × 179.

Fig. 5. Grade +++ observed in an animal of group A, killed 207 days after operation. × 179.

Fig. 6. Section of a nerve from group B (section plus ligature). Observe the passage of nerve fibers over the ligature with intercrossing of neurofibrils on both sides. × 63.

Figs. 7 and 8. Further detail of the same process. × 179.

[1]All photomicrographs are of nerve sections stained by Ranson's method.

In the group of animals treated with gentian violet the absence of neuromas was verified only in one-third of the cases. These results are not so satisfactory as those found by Poth and associates, Guttmann and Medawar, and Padovani and Mansuy (22).

Our results with formaldehyde have shown that in approximately 70 per cent of the cases neuromas of great density (++ and +++) have formed. Thus, the inhibition of the nerve stump was not as successful as described by Guttmann and Medawar.

The treatment with absolute alcohol proposed by Huber and Lewis prevented neuroma formation in our material in only one-sixth of the cases. Our opinion agrees, therefore, with that of Poth and associates and Cieslak and Stout that this method is not to be recommended.

Histologic study showed that treatment of the stump with alcohol, formalin, or gentian violet after section and ligature does not prevent neuroma nor neurofibrillar growth over the ligature (Figs. 11 and 12).

The method used by Dogliotti, Teneff, and Micheli, Tomoff, Moszkowicz in which the nerve stump is implanted into the muscle host has recently been the object of an experimental study by Teneff. Our results were poor, for in approximately half of the instances a neuroma of great density (+++) was observed. It is interesting to observe that

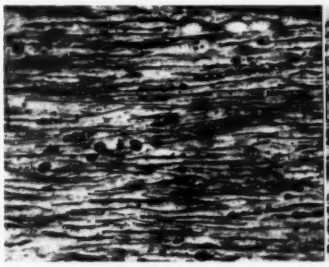

Fig. 9.

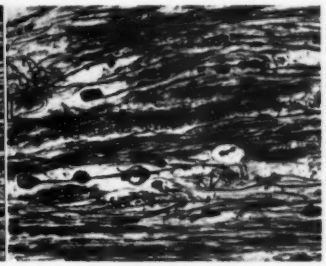

Fig. 10.

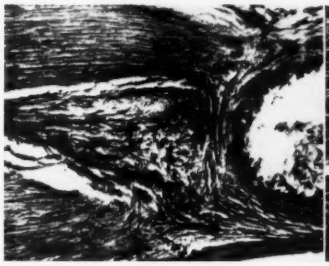

Fig. 11.

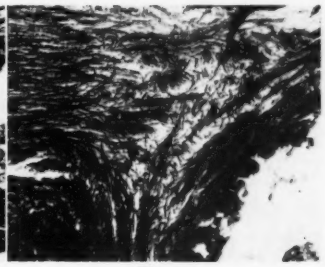

Fig. 12.

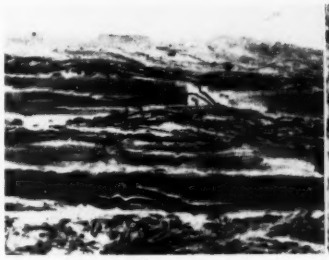

Fig. 13.

Fig. 14.

Figs. 9 and 10. Section of a nerve from group B (section plus ligature). Observe coiling, beading, ballooning, and spiral aspects of neurofibrils due to the nerve ligature. × 357.

Figs. 11 and 12. A grade +++ neuroma developed in a nerve of group G (gentian violet). × 62 and 178.

Figs. 13 and 14. Neurofibril invasion of striated muscle in animals of group B (section plus ligature). × 357 and 178.

neurofibrils occasionally proliferate growing into the neighboring muscular tissue despite the nerve having been ligated and not implanted into this tissue (Figs. 13 and 14).

Of the methods studied, the one that gave the best results in our experiments was the method applied in group F, in which besides the utilization of gentian violet and tannic acid, a collodium cuff was formed around the stump. The basis of this technique lies in the fact that it is necessary to add to the early inhibitory action of gentian violet, the delayed action of tannic acid and the physical protection of the stump with a substance like collodium. Since the proliferation of neurofibrils is apparently directly related to the nerve cell body, it is practically impossible to obtain inhibition of neurofibrillar proliferation, and the prevention methods should be based on means which can inhibit the pro-

liferation of the connective tissue as much as possible. This method in our material gave the best results of all groups, as dense neuroma formation (degrees ++ and +++) was prevented in more than 80 per cent of the cases. Further observations with this method in other species are desirable in order to furnish additional data that would enable its utilization in human patients.

SUMMARY

The authors stress the necessity of a comparative study of the techniques for the prevention of amputation neuroma and present the results of an experimental research. The sciatic nerves of rats were sectioned, the proximal stump was treated by 9 different methods and submitted to an observation period ranging from 50 to 378 days. A histologic study was undertaken in order to compare the density of the neuromas found. The best results were obtained by ligating the nerve, injecting with gentian violet, and covering with tannic acid powder and collodium.

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CONTINENCE-PRESERVING PROCEDURES IN THE TREATMENT OF CARCINOMA OF THE MIDDLE AND UPPER PARTS OF THE RECTUM

COMBINED abdominoperineal resection became the standard treatment of carcinoma of the rectum and rectosigmoid in English-speaking countries soon after its introduction by Miles in 1908. While continence-preserving procedures continued to be employed in Europe, it was not until the early 1930's that procedures of the pull-through type were reintroduced in the United States by Babcock. At about the same time, Dixon and others began to treat lesions of the upper part of the rectum by means of low anterior resection. Neither type of procedure proved particularly acceptable until some 10 years later, at a time when colonic resections of all types had become materially safer.

Experience with the continence-preserving procedures has by now been sufficiently adequate to permit their critical evaluation. It has been contended that they are more difficult technically and more hazardous than combined abdominoperineal resection; that fecal control after sphincter-saving procedures is little different from that achieved with abdominal colostomy; and, finally, that they are less radical and hence less adequate in dealing with a malignant lesion than is combined abdominoperineal resection. The three criticisms will be discussed separately in the light of the experience of the last decade.

The first criticism, having to do with technical difficulties and hazards, is largely historic. Before the use of chemotherapy and antibiotics, pelvic abscesses were distressingly frequent and often fatal after procedures of either type. It was chiefly because of this complication that the procedures found so little favor prior to the last 10 years. Adequate preparation with antibiotics and their use during the early postoperative period have not only reduced the incidence of local infections, but have also made such infections largely innocuous. At present, the continence-preserving procedures can be carried out with no greater and probably with less risk than that associated with combined abdominoperineal resection.

The supposed technical difficulties have clearly been overemphasized. The anastomosis after low anterior resection becomes difficult only when it is attempted deeply within a narrow pelvis. In such cases, it is possible to avoid the difficulty completely by using a procedure of the pull-through type, in which the anastomosis is achieved without the need of suturing. Sloughing of the telescoped proximal bowel is still occasionally observed

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after pull-through procedures. In the great majority of cases circulation through the marginal artery proves adequate, and, in all cases, the integrity of the arterial supply can be ascertained before continuing with the procedure. Rarely, an adequate length of vascularized bowel cannot be secured, precluding the use of the procedure. If reasonable precautions are observed, the problem of sloughing is not serious.

The criticism having to do with fecal control after pull-through procedures has also been resolved. Normal fecal control is dependent on a reflex the receptors of which are in the wall of the rectum. It is not known whether they are located in the mucosa or in the muscular wall. Cocainization of the mucosa abolishes the reflex, however. If the rectum is removed, the reflex is abolished and normal control is lost. If as little as 3 or 4 centimeters of the most distal part of the intact rectum, as measured upward from the dentate line, is saved, fecal control is retained to the degree that diet, enemas or physics, or a protective pad is unnecessary. With shorter lengths of rectum, the degree of fecal control retained is directly proportional to the length of the rectal stump. If the sphincter only is saved, normal control is lost. However, the sphincter, which has tone and which can be contracted at will, provides some control as does the plastic enlargement of the bowel which occurs to accommodate a fecal mass. The distention and enlargement of the bowel produces a sensation which warns the individual of an impending movement. The degree of control is almost never sufficient to dispense with a protective pad and is quite inadequate if the stool is liquid. A surprising degree of continence may be achieved by a constipating diet and regular irrigations.

The remaining criticism of the continence-preserving procedures, that they are less adequate in dealing with carcinoma than is the procedure of Miles, still has some pertinence. Actually, the controversy has to do with the treatment of lesions in a most limited segment of the rectum. When it became known that lateral lymphatic spread occurs primarily with lesions of the lower 4 centimeters of rectum, it was obvious that wide lateral resections, including removal of the levators, sphincter, and pararectal tissues, were mandatory for adequate treatment of lesions at this level. It is agreed at present that the continence-preserving procedures should not be employed to treat lesions of the lower 5 or 6 centimeters of the rectum. The treatment of lesions of and above the rectosigmoid has also become standardized to the extent that some type of segmental resection is almost invariably employed, in place of combined abdominoperineal resection. The debate over treatment thus has to do only with lesions from 6 to perhaps 10 or 12 centimeters above the dentate margin.

Numerous studies of lymphatic spread of carcinoma of this segment of the rectum have shown that primary lateral lymphatic spread does not occur. Retrograde spread is most limited until after proximal lymphatics have become blocked. Even in such cases involved nodes have practically never been found more than 3 or 4 centimeters below the lower margin of the lesion. Intramural spread similarly is limited. Except in the case of unusual anaplastic lesions, spread more than 1 centimeter beyond the apparent edge of the lesion (2 cm. as measured on the bowel before resection) has not been observed. The findings regarding local spread all indicate that resection of perhaps 5 centimeters of rectum and pararectal tissues below the lesion should be quite adequate. There can be no debate over any difference in the adequacy of the resection proximally and laterally since the extent of

the resection can and should be made the same whether segmental resection, a pull-through procedure, or combined abdominoperineal resection is carried out.

Further and probably more direct evidence that the continence-preserving procedures are as curative as combined abdominoperineal resection is that the late survival rates are comparable regardless of which type of procedure is employed. For lesions of the mid-rectum, after sphincter-saving procedures specifically, the 5 year survival rate is somewhat better than 50 per cent. Without involvement of lymph nodes the corresponding rate is approximately 70 per cent, whereas with nodal involvement it is 30 per cent. These rates are well within the range currently being reported after combined abdominoperineal resection of similar lesions of the same segment of rectum. Even better results may be expected after resection of lesions above this level. As previously discussed, the treatment of lesions higher than 10 to 12 centimeters above the dentate line is no longer controversial since some type of segmental resection is employed generally.

It probably can be concluded safely that results are comparable after treatment of carcinoma of the middle and upper parts of the rectum whether continence is preserved or sacrificed. If this is so, there would seem to be little reason for the continued use of the more mutilating procedure.

B. Marden Black.

THE SURGEON AT WORK

A COMPARISON OF THE MICROTECHNIQUE AND MACROTECHNIQUE FOR BLOOD VOLUME DETERMINATIONS

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NUMEROUS reports have appeared describing various methods of plasma and blood volume determinations. In recent years, the majority of these reports have been concerned with tagging one of the blood elements with a radioactive isotope and performing isotopic dilution studies to determine the plasma volume or the red cell mass. Red cell mass has been determined by tagging erythrocytes with radioactive phosphorus, iron, and chromium while plasma volume determinations have been performed by tagging human serum albumin with radioactive iodine. These studies have been made previously by utilizing venous blood samples and performing radioassays by means of macromethods with samples containing 5 to 10 milliliters of blood.

It has been apparent that in many seriously ill patients it is impossible to perform repeated venipunctures, because of the lack of suitable veins. Whereas interns or more qualified personnel are usually required to make a venipuncture in such a patient, technicians will experience no difficulty in performing a finger puncture. Following a suggestion of M. C. Reder, a method of determining the total blood and plasma volume from capillary blood was attempted.

The results of plasma and blood volume determination by a microtechnique are here compared with results of a simultaneous standard macroprocedure of plasma and blood volume determination.

This study was supported by the Office of the Surgeon General, Department of the Navy.

The opinions expressed herein are those of the authors and not necessarily those of the Department of the Navy.

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MATERIAL AND METHODS

The subjects of this study were patients admitted for elective surgery to the surgical service of the U. S. Naval Hospital, Bethesda, Maryland, and hospital corpsmen and corp Waves attached to the same institution. Simultaneous plasma and total blood volumes were determined by the microtechnique and macrotechnique in 24 males and 10 females. Iodinated (I^{131}) human serum albumin was used in both instances. The standard macroprocedure for the determination of the plasma volumes has been previously described (1).

An amount of iodinated human serum albumin having an activity of 25 to 50 microcuries is injected into the antecubital vein. Ten minutes later a finger puncture is performed on the same side used for injection. The puncture is made deep enough to insure a free flow of blood. The blood sample for hematocrit determination by the microtechnique is obtained from the finger puncture with a heparinized capillary tube, 75 millimeters in length, filled by capillary action to approximately three-quarters of its length. One end is then flame-sealed and the tube centrifuged for 30 minutes at 3,000 revolutions per minute. As described by Gregersen, a correction factor of 0.96 is used for the hematocrit determination by microtechnique to compensate for plasma trapped among the packed red cells.

One-tenth milliliter of capillary blood is drawn in a 0.2 milliliter (TC) heparinized pipette. This is transferred to a 10 milliliter test tube. As a routine procedure after each transfer, the pipette is flushed 4 times with distilled water and the washings added to the primary solution. The volume is then made up to 2.0 milliliters by the addition of distilled water. A radioassay is performed on the contents of the 10 milliliter test tube with a scintillation counter utilizing a well-type sodium iodide

crystal. This type of counter allows the maximum sensitivity of a crystal counter with geometry closely approaching 4 pi, since the volume counted fills less than 50 per cent of the depth of the well.

A 0.1 milliliter aliquot of the standard previously prepared by dilution of the iodinated human serum albumin is transferred to a 10 milliliter test tube in the same manner as already described and the volume made up to 2.0 milliliters with distilled water. This is also counted in the scintillation counter.

The total blood volume is then calculated by the micromethod:

$$\text{T.B.V.} = \frac{\text{Activity standard} \times \text{volume injected} \times \text{dilution of standard}}{\text{Activity of specimen}}$$

The plasma volume is then estimated by the microtechnique:

$$\text{P.V.} = (\text{T.B.V.}) \times (1 - \text{corrected hematocrit})$$

At the same time that the finger puncture is performed, approximately 10 milliliters of blood are withdrawn from the opposite antecubital vein for plasma and blood volume determination using the standard 1 sample macrotechnique (2). The sample is centrifuged for 30 minutes at 3,000 revolutions per minute. Duplicate 2 milliliter specimens of plasma are counted by means of a mica end window Geiger tube. Duplicate 2 milliliter samples of the same standard used in the microtechnique are counted in the same manner.

The plasma volume is then calculated by the macromethod:

$$\text{P.V.} = \frac{\text{Activity standard} \times \text{volume injected} \times \text{dilution of standard}}{\text{Activity of sample}}$$

The total blood volume is then estimated by the macrotechnique utilizing the venous hematocrit value corrected by a factor of 0.96:

$$\text{T.B.V.} = \frac{\text{Plasma volume}}{1 - \text{corrected hematocrit}}$$

RESULTS

The mean plasma volume for men using the standard 1 sample macrotechnique was 43.7 milliliters per kilogram of body weight (standard deviation of 5.3) (Table I). Estimated by the microtechnique the mean plasma volume was 46.1 milliliters per kilogram of body weight (standard deviation of 5.0).

The mean total blood volume for men with the standard macrotechnique was 78.7 milliliters per kilogram of body weight (standard deviation of 10.9). By the microtechnique it was 80.6 milliliters per kilogram of body weight (standard deviation of 9.7).

TABLE I.—COMPARISON OF MICROTECHNIQUE AND MACROTECHNIQUE FOR BLOOD VOLUME DETERMINATIONS IN NORMAL HUMAN MALES

Case No.	Age (yr.)	Weight (kgm.)	Microtechnique			Macrotechnique		
			Corrected hematocrit	Plasma vol., ml./kgm.	Total blood vol., ml./kgm.	Corrected hematocrit	Plasma vol., ml./kgm.	Total blood vol., ml./kgm.
1	19	77.3	.326	49.0	73.2	.347	47.4	72.7
2	29	71.8	.358	49.7	77.5	.365	47.2	74.3
3	37	60.5	.399	37.2	62.0	.407	39.7	66.9
4	23	81.8	.417	43.7	75.0	.413	38.7	65.9
5	29	75.9	.448	37.4	66.5	.485	37.2	72.2
6	21	88.6	.369	50.9	80.6	.394	44.4	73.3
7	41	49.1	.438	54.5	97.0	.456	54.4	99.9
8	33	95.5	.433	41.4	72.8	.413	36.1	61.5
9	27	86.4	.389	38.2	62.6	.394	39.8	65.7
10	21	79.5	.438	48.5	86.4	.490	44.3	88.5
11	28	68.2	.422	49.0	85.0	.446	52.1	94.0
12	23	75.0	.420	51.3	88.4	.451	45.0	82.0
13	21	80.0	.472	44.7	84.7	.490	39.2	76.9
14	22	93.2	.462	44.4	82.6	.480	43.0	82.7
15	20	60.0	.418	55.3	95.0	.432	53.2	93.7
16	25	75.5	.437	51.1	90.7	.480	45.6	87.7
17	28	51.4	.470	50.7	95.6	.490	48.9	95.8
18	24	75.5	.480	47.1	90.6	.480	45.6	87.7
19	38	84.6	.490	44.4	87.1	.490	40.6	79.6
20	24	67.2	.403	47.0	78.7	.425	49.5	86.0
21	21	81.8	.413	39.9	68.0	.437	43.4	75.8
22	22	88.2	.440	42.9	76.5	.451	36.5	66.5
23	23	75.0	.467	42.6	79.8	.463	40.6	75.5
24	19	77.3	.419	45.7	78.7	.426	36.0	63.3
				46.1	80.6	Mean	43.7	78.7
				5.0	9.7	Standard deviation	5.3	10.9

The mean plasma volume for women using the standard macrotechnique was 45.2 milliliters per kilogram of body weight (standard deviation of 6.0) (Table II). For the microtechnique it was 45.7 milliliters per kilogram of body weight (standard deviation of 6.7).

The mean total blood volume for women by the standard technique was 74.9 milliliters per kilogram of body weight (standard deviation of 8.2). By the microtechnique it was 75.3 milliliters per

TABLE II.—COMPARISON OF MICROTECHNIQUE AND MACROTECHNIQUE FOR BLOOD VOLUME DETERMINATIONS IN NORMAL HUMAN FEMALES

Case No.	Age (yr.)	Weight (kgm.)	Microtechnique			Macrotechnique		
			Corrected hematocrit	Plasma vol., ml./kgm.	Total blood vol., ml./kgm.	Corrected hematocrit	Plasma vol., ml./kgm.	Total blood vol., ml./kgm.
1	20	61.8	.401	43.2	72.1	.364	45.8	72.1
2	37	46.3	.428	53.0	92.7	.442	51.0	91.5
3	57	52.7	.292	55.6	78.6	.292	55.0	77.6
4	36	60.0	.407	36.0	60.7	.402	38.5	64.4
5	24	62.0	.405	44.2	74.3	.391	49.4	81.1
6	19	64.1	.394	53.8	88.8	.398	49.5	82.3
7	57	70.5	.424	39.7	68.9	.471	35.2	66.5
8	32	55.0	.354	46.9	72.6	.396	45.6	75.4
9	34	67.3	.396	47.9	79.2	.396	43.7	72.4
10	46	68.2	.434	36.7	64.9	.416	38.4	65.2
				45.7	75.3	Mean	45.2	74.9
				6.7	9.4	Standard deviation	6.0	8.2

kilogram of body weight (standard deviation of 9.4).

For every instance mentioned the value for any individual determination fell within 3 standard deviations of the mean for the group.

The coefficient of correlation between the values for the plasma volumes in men as determined by the microprocedure and macroprocedure is 0.79. The coefficient of correlation between the values for the total blood volumes in men as determined by the two methods is 0.82.

In the series of females the coefficient of correlation between the values for the plasma volumes as determined by the two techniques is 0.88 and between the values for the total blood volume is 0.91.

DISCUSSION

The microtechnique gives values for the plasma and total blood volume comparable to those obtained by using the standard 1 sample macrotechnique.

Although the correlation coefficients are not as high as desired, they are still biologically and statistically significant. A probable contributing factor to the lowering of coefficients of correlation in both series is the fact that the standard macroprocedure measures directly the plasma volume whereas the microtechnique measures directly the total blood volume and a comparison of these values involves the use of hematocrit values obtained from different sources.

The ease with which the microtechnique may be performed recommends its use clinically in children, in seriously ill adults with poor veins, and in other instances when it is difficult or undesirable to perform repeated venipuncture or remove a large sample of blood. However, it must be recognized that these studies performed on normal subjects do not establish, without further study, that the micromethod will be equally acceptable under pathologic conditions associated with marked depression of peripheral capillary circulation.

SUMMARY

1. The macrotechnique and microtechnique for determining plasma and total blood volumes by utilizing iodinated (I^{131}) human serum albumin have been compared in a series of 24 human males and 10 human females.

2. The microtechnique utilizing capillary blood gives values for the plasma and total blood volumes favorably comparable to those obtained by using the standard 1 sample macrotechnique.

3. The microtechnique lends itself well to clinical use in patients in whom repeated venipunctures are difficult or undesirable.

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THE SURGEON'S LIBRARY

REVIEWS OF NEW BOOKS

THE volume entitled *Global Epidemiology; a Geography of Disease and Sanitation; the Near and Middle East*[1] is the third in a series of 5 volumes dealing with global epidemiology, the first of which covered India, the Far East, and the Pacific Area. The second dealt with the continent of Africa, and the remaining two volumes will present Europe and Latin America. The purpose of the 5 volumes "is to provide a brief but comprehensive summary of the disease hazards in these countries and to indicate the major factors—environmental, racial, social, economic, and medical—which affect the health and the well being of the inhabitants."

The authors have drawn upon the extensive medical intelligence of the Armed Forces accumulated during and since the last world war, and in addition, through personal visits, various communications, and publications, they have supplemented and brought up-to-date the accumulated health knowledge of the Middle East.

The book reviews the geography and climate, population and socio-economic conditions, environment and sanitation, health services and medical facilities, and the important diseases of 17 geographic areas of the Eastern Mediterranean, Arabian Peninsula, and Southwestern Asia.

The book is divided into 3 sections, the first covers the Near East: Cyprus, Iraq, Israel, Jordan, Lebanon, and Syria. In section 2, those countries of the approaches to Eastern Asia and Europe are discussed: Afghanistan, Iran, and Turkey. The third section deals with the political subdivisions of the Arabian Peninsula: Aden Colony and Protectorate, Bahrain, Kuwait, Muscat and Omar, Qatar, Saudi Arabia, Trucial Oman, and Yemen.

A very valuable appendix accompanies the text giving health hints for travelers and visitors to this part of the world.

The volume on the Near East and the Middle East presents a surprisingly accurate and comprehensive summary of the known health hazards in this part of the world.

The authors are to be commended for compiling and condensing this very valuable information into a concise and interesting publication. The medical and public health professions and the many international health and welfare agencies will find these 5 books indispensable. It is hoped that the authors and the publication will be able to produce subsequent editions as new and important information accumulates in the years to come.

LELAND E. POWERS.

[1]GLOBAL EPIDEMIOLOGY; A GEOGRAPHY OF DISEASE AND SANITATION. By James Stevens Simmons, B.S., M.D., Ph.D., Dr. P.H., Sc.D. (Hon.), Tom F. Whayne, A.B., M.D., M.P.H., Dr.P.H., Gaylord W. Anderson, A.B., M.D., Dr.P.H., and Harold Maclachlan Horack, B.S., M.D. Associate author, Ruth Alida Thomas, B.A., A.M., M.P.H., and collaborators. Vol. 3. THE NEAR AND MIDDLE EAST. 357 pages, illustrated. $12.00. Philadelphia, London, Montreal: J. B. Lippincott Co., 1954.

A RATIONAL and objective approach to the diagnosis and treatment of endocrine disorders entitled *Clinical Endocrinology*[2] is presented for the first time in a complete and integrated volume. During the past decade, there has developed a rapid and more complete understanding of endocrine physiology, thus allowing the field of endocrinology to take its rightful place as a full-fledged member of the group of medical specialties, along with such fields as cardiology, gastroenterology, and allergy. This book is beautifully integrated as the result of a co-operative effort of the biochemist, physiologist, and the clinical endocrinologist, each author being a recognized authority in his respective field. Textbooks of other medical specialties could be greatly improved if they, too, were presented as a joint endeavor of preclinical and clinical authorities.

Clinical endocrinologic disorders can only be understood if the student has a thorough foundation in fundamental endocrine physiology. This aspect is emphasized in this volume, for the authors have realized that in no other field of medicine is it so important that there be a thorough understanding of the physiology and biochemistry of an organ system before the clinical aspects can be appreciated. Each chapter of this text is devoted to an individual endocrine gland. Normal anatomy and physiology are first discussed, following which the pathologic physiology and clinical aspect of hyperfunction, and then hypofunction, are presented.

Laboratory procedures which are important from the point of view of studying patients with endocrine disorders are discussed in the final chapters of the volume. The principles of these procedures are outlined from the standpoint of interpretation without clouding the reader with technical details of the procedure. One chapter is devoted to commercial preparations available for treatment of endocrine disorders. A chapter concerning the newer concepts of understanding the treatment of obesity is especially helpful.

[2]CLINICAL ENDOCRINOLOGY. By Karl E. Paschkis, M.D., Abraham E. Rakoff, M.D., and Abraham Cantarow, M.D. 830 pages, 253 illustrations, 5 in full color. $16.00. New York: Paul B. Hoeber, Inc., Medical Book Department of Harper & Bros. 1954.

This book is well organized, well written and illustrated, and is highly recommended for an up-to-date textbook of clinical endocrinology, both for the student and the clinician. HOWARD A. LINDBERG.

THE first loose-leaf volume on the subject of cytologic diagnosis is presented in *Atlas of Exfoliative Cytology*[1] by Papanicolaou. According to the publisher, Harvard University Press, there will be supplements for which one may subscribe. Some of the expense and the arrangements have been contributed by the Commonwealth Fund.

The first 56 pages of the volume are devoted to: (1) introduction and short history of cytology; (2) technique of collection, fixation, processing, and staining the specimens; (3) criteria of malignancy, discussion of sources of error, and classification of cytologic findings; (4) discussion of the normal, atypical and malignant cytology of the female genital system, urinary and male genital systems, respiratory system, digestive system, breast secretions, and pleural, peritoneal, and pericardial exudates.

[1]ATLAS OF EXFOLIATIVE CYTOLOGY. By George N. Papanicolaou, M.D., Ph.D. 56 pages, and 36 colored plates. $18.00. Cambridge, Mass.: Published for the Commonwealth Fund by the Harvard University Press, 1954.

The remainder of the atlas consists of 36 color plates and a correlating description adjacent to each plate for the various systems listed, plus a miscellaneous chapter, picturing and describing histiocytes; cells from vaginal, endocervical, and urine sediment smears in cases of pregnancy and from an amnion scraping smear; cells showing effects of irradiation; multinucleated cells, and mitotic figures. The bibliography and index complete the text.

The binding is a heavy, pliable plastic material of the loose-leaf type with seven large rings. The paper is heavy and the print is pleasing and clear. The color plates are outstanding.

The only confusing aspect of the volume concerns the references to the color plate numbers given in the discussion. Because this is a loose-leaf atlas designed to permit the addition of new material, it is not feasible to number the pages consecutively. Tab dividers would be an aid.

The author has attained the scope desired: "—first; to illustrate in a uniform manner, the most significant and representative types of exfoliated cells as a basis for an adequate comparative evaluation; and second; to provide a description and discussion of their general or specific diagnostic significance." MARK C. WHEELOCK.

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

ARCHIVIO "PUTTI" DI CHIRURGIA DEGLI ORGANI DI MOVIMENTO. Directto da O. Scaglietti. Redatto da L. Gui. Vol. 4. 563 pages, bibliography 140 pages, illustrated. Florence: Edizioni Scientifiche Dell'—Istituto Ortopedico Toscano, 1954.

PROCEEDINGS OF THE SECOND NATIONAL CANCER CONFERENCE. Vols. 1 and 2. American Cancer Society, Inc. National Cancer Institute of the U. S. Public Health Service and American Association for Cancer Research. Netherland Plaza Hotel, Cincinnati, Ohio, March 3, 4, 5, 1952. 1687 pages, illustrated. $7.50. New York: American Cancer Society, Inc., 1954.

THE PHYSICIAN AND HIS PRACTICE. Edited by Joseph Garland, M.D. 270 pages. $5.00. Boston and Toronto: Little, Brown and Co., 1954.

OFFICE GYNECOLOGY. By J. P. Greenhill, B.S., M.D., F.A.C.S., F.I.C.S. 6th ed., rev. and enl. 517 pages, 127 illustrations. $7.75. Chicago: Year Book Publishers, Inc., 1954.

ROENTGEN-DIAGNOSTICS. By H. R. Schinz, W. E. Baensch, E. Friedl, and E. Uehlinger. 1st American edition based on the 5th German edition. English translation arranged and edited by James T. Case, M.D., D.M.R.E. (Camb.). Cumulative Index. 103 pages. $10.00. New York: Grune & Stratton, 1954.

PHYSICAL THERAPY AFTER AMPUTATION; THE TREATMENT OF THE UNILATERAL LOWER-EXTREMITY AMPUTEE. By Margaret Bryce. 93 pages, 14 illustrations. $1.50. Madison, Wisconsin: The University of Wisconsin Press, 1954.

ANATOMY OF THE HUMAN. By Henry Gray, F.R.S. 26th ed. Edited by Charles Mayo Goss, M.D. 1480 pages, 1202 illustrations. $16.00. Philadelphia: Lea & Febiger, 1954.

CEREBROVASCULAR DISEASE. By James Peter Murphy, M.D., Foreword by Percival Bailey, M.D. 408 pages, 128 illustrations. $12.00. Chicago: Year Book Publishers, Inc., 1954.

LEGAL MEDICINE; PATHOLOGY AND TOXICOLOGY. By Thomas A. Gonzales, M.D., Morgan Vance, M.D., Milton Helpern, M.D., and Charles J. Umberger, Ph.D. Introduction by Harrison S. Martland. 2nd ed. 1349 pages, illustrated. $22.00. New York: Appleton-Century-Crofts, Inc., 1954.

METABOLISMO DEL AGUA Y DE LOS ELECTROLITOS. (EN ESTADO NORMAL Y PATOLOGICO.) By Dr. Harry F. Weisberg. Translation by Dr. Manuel Rene Malinow. Foreword by Eduardo Braun Menendez. 276 pages, 10 illustrations. Buenos Aires: Editorial Artecnica, 1954.

CLINICAL CONGRESS OF AMERICAN COLLEGE OF SURGEONS

FRANK GLENN, New York, *President*
ALFRED BLALOCK, Baltimore, *President-Elect*

PRELIMINARY PLANS FOR 40TH CLINICAL CONGRESS CONVENTION HALL, ATLANTIC CITY, NEW JERSEY NOVEMBER 15 TO 19, 1954

THE high purpose of the annual Clinical Congress—to inform and to learn—will be demonstrated again at the forthcoming meeting in Atlantic City, November 15 to 19. To accomplish this aim, the scope of the Congress is widened year by year, in response to the needs and wishes of the Fellows. Because of the high quality and versatility of this year's program, the result of hard, earnest planning, it is believed that this meeting will be one of the most instructive in the history of the College.

New features this year include: an expanded program of postgraduate courses, 8 in all, including 3 in the surgical specialties Gynecology and Obstetrics, Orthopedic Surgery, and Thoracic Surgery; "joint" specialty sessions, of interest to more than one field; 227 Forum papers, 41 more than last year; an unusually distinguished program of films, with many of the authors present to give personal narration; color television emanating from the Hospital of the University of Pennsylvania; many distinguished guest speakers; and more scientific and technical exhibits than ever before.

Headquarters for meetings and exhibits will be Convention Hall, one of the world's largest meeting centers, located on the famous Atlantic City Boardwalk. This is the first Congress ever to be held in this noted resort city, which is celebrating its Centennial Year, 1854–1954.

POSTGRADUATE COURSES

Eight postgraduate courses will be given this year, in the mornings from 8:30 to 11:30, Monday through Thursday. Registration for these popular courses will be limited, so that it is advisable to register in advance. Registration forms may be obtained from the American College of Surgeons, 40 East Erie Street, Chicago 11, Illinois. The fee is $5.00 per course. Courses are progressive, so that one can register for one course only. The program appears on the following pages.

COLOR TELEVISION

Through the courtesy of Smith, Kline & French Laboratories, of Philadelphia, an outstanding color television program will again be a highlight of the Congress. Under the leadership of Dr. I. S. Ravdin of Philadelphia, the programs will be presented November 15 through 19, and will consist of operative clinics and dry clinics, emanating from the Hospital of the University of Pennsylvania, and transmitted over a microwave link to Convention Hall. A number of Philadelphia surgeons will be operating. Reception will be better than ever before, with two large screen receivers on the floor of the Hall. These receivers are equipped with 4½ by 6 foot video screens and together are capable of accommodating an audience of 1,200 persons.

The schedule of operations will be published in the *Daily Bulletin* of the Congress.

CINÉ CLINICS

Through the courtesy of Davis & Geck Inc. an important program of Ciné clinics are scheduled for each morning, Tuesday through Friday. These film-lectures come from surgeons in Canada and the United States and cover important developments in the field. Under the guidance of Dr. Hilger Perry Jenkins, Chairman, and his Medical Motion Picture Committee, the following program has been planned:

Diaphragmatic Hiatus Hernia. BRIAN B. BLADES, Washington, D. C.
Subphrenic Abscess. H. H. BRADSHAW, Winston-Salem.

Hysterectomy. JOHN C. BURCH, M.D., Nashville.
Cholecystectomy. RICHARD B. CATTELL, Boston.
Duodenal Ulcer. ROBERT J. COFFEY, Washington.
Resection of the Colon for Carcinoma. WARREN H. COLE, Chicago.
Acute Head Injuries. LOYAL DAVIS, Chicago.
Carcinoma of the Breast. DERYL HART, Durham.
Nephrectomy. ROBERT M. JANES, Toronto.
Acute Abdominal Injuries. FREDERICK E. KREDEL, Charleston.
Acute Injuries of the Chest. RUDOLF J. NOER, Louisville.
Cancer of the Stomach. ALTON OCHSNER, New Orleans.
Complicated Appendicitis. J. D. RIVES, New Orleans.
Biliary Atresia. ROBERT T. TIDRICK, Iowa City.
Volvulus of the Intestine. HARWELL WILSON, Memphis.
Bilroth I Gastrectomy. ROBERT M. ZOLLINGER and EDWIN H. ELLISON, Columbus.
Arteriovenous Fistula. HARRIS B. SHUMACKER, JR., Indianapolis.

MEDICAL MOTION PICTURES

Congress visitors will find that the Medical Motion Picture program planned by the Committee on Medical Motion Pictures will be more profitable than ever before. The program will be made up of excellent teaching films, and many of the authors will be on hand to give narration and answer questions.

Films are scheduled for mornings and afternoons each day, and Wednesday and Thursday evenings, and will be shown in more spacious quarters than in the past. The program will be listed in detail in the Congress *Official Program* and the *Daily Bulletin*. Following is a partial list of some of the high points of the program:

Monday:
Surgery of the Intestines. Surgery of Head and Neck.
Tuesday:
Films by specialists in Obstetrics and Gynecology, and Urology, which will be of interest to both groups.
Also films of interest to the specialties of Ophthalmology and Otolaryngology.
Wednesday:
Surgery of the Liver, Biliary Tract and Pancreas.
Thursday:
A series of films of interest to Plastic and Orthopedic Surgeons. Cardiovascular Surgery.
Motion Picture Symposium, to be held in the evening, on Spectacular Lesions in Surgery. CHARLES W. MAYO, Rochester, Minnesota, presiding.
Friday:
Thoracic Surgery.

FORUM ON FUNDAMENTAL SURGICAL PROBLEMS

Because the Forum on Fundamental Surgical Problems continues to be an exceptionally distinguished and popular program, this year's sessions have been increased to 20 as compared to 16 last year. Seven sessions will be devoted exclusively to special fields of surgery, including anesthesiology. Forum sessions will be held Monday through Thursday, mornings and afternoons.

A new session has been added this year, on Friday morning, entitled "What's New in Surgery?" At this meeting a number of presiding officers of the Forum sessions will summarize the high spots of research in their respective fields, conducted during the current year and reported at the Forum during Congress week. Dr. I. S. Ravdin, Chairman of the Surgical Forum Committee, reports that representatives of five special fields of surgery were added to the membership of the Forum Committee this year. Authors and papers are listed on following pages.

EVENING SESSIONS

Two general evening sessions have been planned this year, on Monday and Friday. Special meetings, including medical motion pictures in ophthalmology on Wednesday and Thursday evening and the Motion Picture Symposium on Thursday evening, are also scheduled. Dr. Frank Glenn, President, will preside over the Presidential Meeting on Monday evening, at which Dr. Charles H. deT. Shivers, Chairman of the Atlantic City Advisory Committee on Arrangements, will give the Address of Welcome, Dr. Evarts A. Graham will introduce the guests of the evening, Dr. Robert H. Kennedy will give the Oration on Trauma, and Dr. Alan Gregg will give the Ninth Martin Memorial Lecture, speaking on "Horizons at Half Century." On Friday evening new Fellows will be received into the College, Honorary Fellowships conferred, and Dr. Alfred Blalock will make his incoming Presidential Address.

ADVANCE RESERVATIONS

All official registration forms—advance registration, postgraduate courses, transportation, and hotel accommodations—must be obtained from The American College of Surgeons, 40 East Erie Street, Chicago 11, Illinois. The advantages of advance planning are twofold: you are handed your badge and tickets immediately on checking in at the Advance Registration Desk, so that there is no waiting in line; and you are more likely to obtain your first choice in courses and accommodations. Scientific sessions will begin promptly on Monday morning, hence it is advisable to register in advance if at all possible.

For the convenience of Congress visitors the official registration desks will be open on Sunday, from 3 to 8 p.m., Monday from 8 a.m. to 7 p.m., and Tuesday through Friday from 8 a.m. to 5 p.m.

No registration fee is charged Fellows whose dues are paid as of December 31, 1953; no registration fee is required of Initiates, Junior Candidates, or Surgical Residents whose applications are ac-

companied by a letter of identification from the chief surgeon or hospital administrator. Non-Fellows will pay $20.00 and members of the Federal Services $10.00.

A preliminary program of the Congress follows. The complete program will be published and will be available in the November issue of the College *Bulletin*.

PROGRAM IN BRIEF

Monday, November 15, 1954

8:30–11:30 Postgraduate Courses:
Cardiovascular Surgery
Preoperative and Postoperative Care
Surgery of the Lower Esophagus, Stomach, and Duodenum
Diseases of the Liver, Biliary Tract, and Pancreas
Gynecology and Obstetrics
Orthopedic Surgery—Lower Extremity Amputations and Prostheses
Thoracic Surgery—Surgical Aspects of Pulmonary Disease
Combined Injuries to the Extremities
9:00–12:00 Forums: Heart. Metabolism
9:00–12:00 Medical Motion Pictures (Surgical Specialties)
9:00–12:00 Television
10:00–12:00 Panel: Benign Lesions of Lower Esophagus
1:30– 3:00 Clinicopathology Conference
1:30– 5:30 Medical Motion Pictures
2:00– 4:00 Television
2:00– 5:00 Forums: Blood Circulation. Vital Staining of Lymphatics. Urology. Burns
3:30– 5:00 Panel Discussion: Diverticulitis
8:30–10:00 President's Evening

Tuesday, November 16, 1954

8:30–11:30 Postgraduate Courses: Same as Monday
9:00–12:00 Television
9:00–12:00 Forums: Vascular Grafts. Anesthesia and Postoperative Problems. Cancer
9:00–10:30 Medical Motion Pictures (Otolaryngology)
9:00–12:00 Medical Motion Pictures (Surgical Specialties)
9:00–12:30 Ciné Clinic
1:00– 3:00 Panel Discussion: Surgical Management of Diseases of the Cornea
1:30– 3:00 Panel Discussion: Hypothermia
1:30– 5:30 Medical Motion Pictures
2:00– 4:00 Television
2:00– 5:00 Symposium on Trauma
2:00– 5:00 Forums: Pancreas. Cardiovascular. Obstetrics and Gynecology
3:30– 5:00 Panels: Hormonal Balance in Surgery. Relationship of Blood Dyscrasias to Otolaryngology and the Control of Bleeding
8:00–10:00 Medical Motion Pictures (Ophthalmology)
8:30–10:30 Program of Professional Entertainment

Wednesday, November 17, 1954

8:30–11:30 Postgraduate Courses: Same as Monday
9:00–10:30 Panel: Urology. The Clinical Management of Spinal Cord Injuries
9:00–10:30 Symposium: Otolaryngology — Larynx, Mouth, and Tongue
9:00–12:00 Medical Motion Pictures (Surgical Specialties)
9:00–12:00 Television
9:00–12:00 Forums: Lung, Wounds, and Infection. Gastrointestinal Tract. Steroids
9:00–12:30 Ciné Clinic
10:45–12:00 Scientific Session: Otolaryngology
10:45–12:15 Panel: Urology—Incontinence in Women
1:00– 3:00 Panel: Ophthalmology—Minor Surgical Problems of the Eye and Adnexae
1:30– 3:00 Clinicopathology Conference
1:30– 3:00 Panel Discussion: Gynecology and Obstetrics. Urologic Injuries in Pelvic Surgery, Their Prevention and Treatment
1:30– 5:30 Medical Motion Pictures
2:00– 4:00 Television
2:00– 5:00 Symposium on Cancer
2:00– 5:00 Forums: Nutrition. Orthopedic
3:30– 5:00 Panels: Peripheral Arterial Disease. Gynecology and Obstetrics—Differential Diagnosis and Treatment of Vaginal Discharges. Otolaryngology—Management of Sinus Disease
6:30–10:00 Dinner Meeting: Medical Schools—Department of Surgery
8:00–10:00 Medical Motion Pictures (Ophthalmology)

Thursday, November 18, 1954

7:30– 9:30 Forum Committee Breakfast
8:30–11:30 Postgraduate Courses: Same as Monday
9:00–12:00 Television
9:00–10:30 Panel: Urology—The Abdominal Mass
9:00–10:30 Symposium: Otolaryngology
9:00–12:00 Forums: Neurosurgery. Liver, Portacaval Anastomosis, and Other Circulatory Problems. Plastic Surgery
9:00–12:00 Medical Motion Pictures (Surgical Specialties)
9:00–12:30 Ciné Clinic
10:45–12:00 Medical Motion Pictures (Otolaryngology)
1:00– 3:00 Panel: Ophthalmology—Selection of Operative Technique in Retinal Separation
1:30– 3:00 Panels: The Use and Abuse of Antibiotics in Therapy. Gynecology and Obstetrics—Perinatal Pathology. Experiences in the Treatment of Intracranial Meningiomas
1:30– 3:00 Symposium: Graduate Training in Surgery
1:30– 3:30 Medical Motion Pictures
2:00– 3:30 Television
3:45– 6:00 Annual Meeting of Fellows
8:00–10:00 Medical Motion Pictures (Ophthalmology)
8:30–10:00 Motion Picture Symposium on Spectacular Surgery
8:30–10:30 Adventures in Science

Friday, November 19, 1954

9:00–12:00 Forum Summary
9:00–12:00 Television
9:00–12:00 Forum: Neurosurgery
9:00–12:00 Medical Motion Pictures (Surgical Specialties)
9:00–12:30 Ciné Clinic
1:30– 3:00 Assembly of Initiates
1:30– 4:45 Panel Discussions: Gynecology and Obstetrics. Neurologic Surgery. Orthopedic Surgery. Plastic Surgery. Thoracic Surgery. Urology
1:30– 5:30 Medical Motion Pictures
8:30–10:00 Convocation

PRELIMINARY PROGRAM

EVENING SESSIONS

PRESIDENT'S EVENING

Monday, 8:30-10:00 p.m., Ballroom, Convention Hall

FRANK GLENN, M.D., F.A.C.S., New York; President, American College of Surgeons, *Presiding.*
Address of Welcome. CHARLES H. DeT. SHIVERS, M.D., F.A.C.S., Atlantic City; Chairman, Advisory Committee on Local Arrangements.
Introduction of Guests. EVARTS A. GRAHAM, M.D., F.A.C.S., St. Louis; Chairman, Board of Regents.
Oration on Trauma. Our Number Three Killer. ROBERT H. KENNEDY, M.D., F.A.C.S., New York.
The Ninth Martin Memorial Lecture: Horizons at Half Century. ALAN GREGG, M.D., New York; Vice President, Rockefeller Foundation.

CONVOCATION

Friday, 8:30–10:00 p.m., Ballroom, Convention Hall

FRANK GLENN, M.D., F.A.C.S., New York; President, American College of Surgeons, *Presiding.*
Procession. Initiates, Governors, Officers, Regents, and Guests.
Invocation.
Installation of New Officers:
Second Vice President: JOHN C. BURCH, M.D., F.A.C.S., Nashville.
First Vice President: WILLIAM L. ESTES, JR., M.D., F.A.C.S., Bethlehem, Pa.
President: ALFRED BLALOCK, M.D., F.A.C.S., Baltimore.
Presentation of Initiates. Chairman of the Board of Regents.
Fellowship Pledge. The Initiates.
Conferring of Fellowships. The President.
Conferring of Honorary Fellowships. The President.
Presidential Address. ALFRED BLALOCK.
Recession.

ANNUAL MEETING—BOARD OF GOVERNORS

Luncheon, Sunday, 10:00 a.m.,–5:00 p.m., Belvedere Room, The Traymore

WILLARD H. PARSONS, M.D., F.A.C.S., Vicksburg, Mississippi; Chairman, Board of Governors, *Presiding.*
Minutes of the 1953 Annual Meeting of the Board of Governors. RICHARD E. AHLQUIST, M.D., F.A.C.S., Spokane; Secretary, Board of Governors.
Report of the Chairman—Résumé of Interim Activities. WILLARD H. PARSONS, M.D., F.A.C.S.
Report of the Executive Committee. RICHARD E. AHLQUIST, M.D., F.A.C.S.
Report of the President. FRANK GLENN, M.D., F.A.C.S., New York.
Report of the Chairman, Board of Regents, EVARTS A. GRAHAM, M.D., F.A.C.S., St. Louis.
Report of the Director. PAUL R. HAWLEY, M.D., F.A.C.S. (Hon.), Chicago.
Report of Committee on Itinerant Surgery and Surgeons. RICHARD E. AHLQUIST, M.D., F.A.C.S., Chairman.
Report of Committee to Develop Instruction to Undergraduate Medical Students Regarding Problems of Ethics. HERBERT WILLY MEYER, M.D., F.A.C.S., New York, Chairman.
Report of Committee to Develop a Concrete and Full Program Toward Interesting Surgical Fellows and Residents in the College. EUGENE J. JOERGENSON, M.D., F.A.C.S., Glendale, Chairman.
Report of Committee to Study the Resolution of the Establishment of a Gynecological Section of the A.C.S. Within the General Surgery Section. JOSEPH F. SHUFFIELD, M.D., F.A.C.S., Little Rock, Chairman.
Report of Committee to Further Study the Method of Selecting Governors. JAMES E. M. THOMSON, M.D., F.A.C.S., Lincoln, Chairman.
Report of the Committee Concerning Increasing the Interest in the College of the Various Sub-Specialty Groups. CHARLES S. HIGGINS, M.D., F.A.C.S., Cleveland, Chairman.
Individual Resolutions by Governors.
Announcements.

ADJOURNED MEETING—BOARD OF GOVERNORS

Thursday, 3:30–3:45 p.m., Ballroom, Convention Hall

WILLARD H. PARSONS, M.D., F.A.C.S., Chairman; *Presiding.*
Report of Committee on Nominations to the Board of Governors.
Report of Nominating Committee on Election of Regents.
Election of Regents of College.
Report of Nominating Committee on Electing of Officers, Board of Governors.
Election of Officers, Board of Governors.
Announcement of Nominating Committee, Board of Governors 1954–1955.
Adjournment.

ANNUAL MEETING OF FELLOWS

Thursday, 3:45–6:00 p.m., Ballroom, Convention Hall

FRANK GLENN, M.D., F.A.C.S., New York; President, *Presiding.*
Call to Order by the President
Election of Officers of the College
Election of Governors of the College
Report of the Treasurer
Report on 1954 Annual Meeting of Board of Governors
Reports on Standing Committees:
- Cancer
- Trauma
- Graduate Training
- Medical Motion Pictures
- Nutrition of Surgical Patient

Reports of Departments, Summary by The Director.
Adjournment.

GENERAL SESSIONS

Monday, 10:00–12:00 noon, Ballroom, Convention Hall

Benign Lesions of the Lower Esophagus
Moderator: RICHARD H. SWEET, M.D., F.A.C.S., Boston.
Collaborators: WILLIAM E. ADAMS, M.D., F.A.C.S., Chicago; THOMAS H. BURFORD, M.D., F.A.C.S., St. Louis; JOHN H. GARLOCK, M.D., F.A.C.S., New York; HERMAN J. MOERSCH, M.D., F.A.C.P., Rochester, Minn.

1:30–3:00 p.m., Ballroom, Convention Hall

Clinicopathology Conference
Moderator: ROBERT C. HORN, JR., M.D., Philadelphia.
Collaborators: WILLIAM T. FITTS, JR., M.D., F.A.C.S., Philadelphia; RICHARD A. KERN, M.D., F.A.C.P., Philadelphia; GEORGE P. ROSEMOND, M.D., F.A.C.S., Philadelphia; FRANCIS C. WOOD, M.D., F.A.C.P., Philadelphia.

3:30–5:00 p.m., Ballroom, Convention Hall

Diverticulitis
Moderator: JOHN M. WAUGH, M.D., F.A.C.S., Rochester, Minn.
Collaborators: ALLEN M. BOYDEN, M.D., F.A.C.S., Portland, Ore.; PAUL H. T. THORLAKSON, M.D., F.A.C.S., Winnipeg; RUPERT B. TURNBULL, JR., M.D., F.A.C.S., Cleveland.

Tuesday, 1:30–3:00 p.m., Ballroom, Convention Hall

Hypothermia
Moderator: WILFRED G. BIGELOW, M.D., F.R.C.S.(C), Toronto.
Collaborators: F. JOHN LEWIS, M.D., F.A.C.S., Minneapolis; WILLIAM H. MULLER, JR., M.D., F.A.C.S., Los Angeles; HENRY SWAN, M.D., F.A.C.S., Denver.

3:30–5:00 p.m., Ballroom, Convention Hall

Hormonal Balance in Surgery
Moderator: HAROLD A. ZINTEL, M.D., F.A.C.S., New York.
Collaborators: CHARLES ECKERT, M.D., F.A.C.S., St. Louis; JAMES D. HARDY, M.D., F.A.C.S., Memphis; J. HARTWELL HARRISON, M.D., F.A.C.S., Boston; MARK A. HAYES, M.D., F.A.C.S., New Haven, Conn.

Wednesday, 1:30–3:00 p.m., Ballroom, Convention Hall

Clinicopathology Conference
Moderator: JOHN M. PEARCE, M.D., New York.
Collaborators: CLAUDE E. FORKNER, M.D., F.A.C.P., New York; FRANK GERBODE, M.D., F.A.C.S., San Francisco; RICHARD WARREN, M.D., F.A.C.S., Brookline.

3:30–5:00 p.m., Ballroom, Convention Hall

Peripheral Arterial Disease
Moderator: MICHAEL E. DEBAKEY, M.D., F.A.C.S., Houston.
Collaborators: FREDERICK W. COOPER, JR., M.D., F.A.C.S., Emory University; GEZA deTAKATS, M.D., F.A.C.S., Chicago; F. A. SIMEONE, M.D., F.A.C.S., Cleveland.

Thursday, 1:30–3:00 p.m., Ballroom, Convention Hall

The Use and Abuse of Antibiotics in Therapy
Moderator: W. A. ALTEMEIER, M.D., F.A.C.S., Cincinnati.
Collaborators: HENRY H. BALCH, JR., Major, MC, USAR, F.A.C.S., Washington, D.C.; HARRY S. MORTON, M.D., F.A.C.S., Montreal; WILLIAM R. SANDUSKY, M.D., F.A.C.S., Charlottesville, Va.

SURGICAL SPECIALTIES

UROLOGY

Wednesday, 9:00–10:30 a.m., American Room, The Traymore

The Clinical Management of Spinal Cord Injuries
Moderator: GEORGE C. PRATHER, JR., M.D., F.A.C.S., Brookline.
Collaborators: Orthopedic Surgery—WILLIAM G. KUHN, JR., M.D., F.A.C.S., New Brunswick; Neurosurgery—FRANK H. MAYFIELD, M.D., F.A.C.S., Cincinnati; Urology—HERBERT S. TALBOT, M.D., F.A.C.S., West Roxbury, Mass.

10:45 a.m.–12:15 p.m., American Room, The Traymore

Incontinence in Women
Moderator: ALBERT E. GOLDSTEIN, M.D., F.A.C.S., Baltimore.
Collaborators: Gynecology—JOHN C. ULLERY, M.D., F.A.C.S., Philadelphia; Neurology—ORTHELLO R. LANGWORTHY, M.D., Baltimore; Urology—ROBERT B. McIVER, M.D., F.A.C.S., Jacksonville.

Thursday, 9:00–10:30 a.m., American Room, The Traymore

The Abdominal Mass
Moderator: ORMOND S. CULP, M.D., F.A.C.S., Rochester, Minn.
Collaborators: General Surgery—ALTON OCHSNER, M.D., F.A.C.S., New Orleans; Gynecology—ROBERT A. KIMBROUGH, JR., M.D., F.A.C.S., Philadelphia; Pathology—ARTHUR PURDY STOUT, M.D., New York; Urology—WILLIAM J. ENGEL, M.D., F.A.C.S., Cleveland.

Friday, 1:30–3:00 p.m., Wedgwood Room, Marlborough Blenheim

Postoperative Depletion States of Urologic Patients
Moderator: GEORGE F. CAHILL, M.D., F.A.C.S., New York.
Collaborators: General Surgery—CARL A. MOYER, M.D., F.A.C.S., St. Louis; Urology—JOHN A. BENJAMIN, M.D., Rochester, N.Y., and HOWARD I. SUBY, M.D., F.A.C.S., Boston.

GYNECOLOGY AND OBSTETRICS

Wednesday, 1:30–3:00 p.m., Wedgwood Room, Marlborough Blenheim

Urologic Injuries in Pelvic Surgery, Their Prevention and Treatment
Moderator: HOWARD ULFELDER, M.D., F.A.C.S., Boston.
Collaborators: Urology—WYLAND F. LEADBETTER, M.D., F.A.C.S., Boston; Gynecology—CONRAD G. COLLINS, M.D., F.A.C.S., New Orleans and HOUSTON S. EVERETT, M.D., Baltimore.

3:30–5:00 p.m., Wedgwood Room, Marlborough Blenheim

Differential Diagnosis and Treatment of Vaginal Discharges
Moderator: WALTER T. DANNREUTHER, M.D., F.A.C.S., New York.
Collaborators: H. CLOSE HESSELTINE, M.D., Chicago; ANDREW A. MARCHETTI, M.D., F.A.C.S., Washington, D.C.; JOHN PARKS M.D., F.A.C.S., Washington, D.C.; WARD F. SEELEY, M.D., F.A.C.S., Detroit.

Thursday, 1:30–3:00 p.m., Wedgwood Room, Marlborough Blenheim

Perinatal Pathology
Moderator: ALLAN C. BARNES, M.D., F.A.C.S., Cleveland.
Collaborators: GEORGE W. ANDERSON, M.D., Baltimore; M. EDWARD DAVIS, M.D., F.A.C.S., Chicago; CHARLES H. HENDRICKS, M.D., F.A.C.S., Cleveland.

Friday, 1:30–3:00 p.m., American Room, The Traymore

Review of Modern Diagnostic Tests of Pregnancy
Moderator: DONALD G. TOLLEFSON, M.D., F.A.C.S., Los Angeles.
Collaborators: EARL T. ENGLE, Ph.D., New York: LOUIS M. HELLMAN, M.D., F.A.C.S., Brooklyn; SOMERS H. STURGIS, M.D., F.A.C.S., Boston.

3:15–4:45 p.m., American Room, The Traymore

Problems of Labor Related to the Myometrium
Moderator: BENJAMIN TENNEY, JR., M.D., F.A.C.S., Boston.
Collaborators: DANIEL J. MCSWEENEY, M.D., F.A.C.S., Brookline; BERNARD J. PISANI, M.D., F.A.C.S., New York; ALFRED L. POTTER, M.D., F.A.C.S., Providence, R.I.

NEUROLOGIC SURGERY

Thursday, 1:30–3:00 p.m., Meeting Room B, Convention Hall

Experiences in the Treatment of Intracranial Meningiomas
Moderator: EDGAR F. FINCHER, M.D., F.A.C.S., Emory University.
Collaborators: FRANCIS C. GRANT, M.D., F.A.C.S., Philadelphia; GILBERT HORRAX, M.D., F.A.C.S., Boston; BRONSON S. RAY, M.D., F.A.C.S., New York.

Friday, 1:30–3:00 p.m., Venetian Room, Ambassador

Electrolyte Balance and Postoperative Infections in the Neurosurgical Patient
Moderator: E. S. GURDJIAN, M.D., F.A.C.S., Detroit.
Collaborators: EDWIN B. BOLDREY, M.D., F.A.C.S., San Francisco; J. LAWRENCE POOL, M.D., F.A.C.S., New York; HENRY G. SCHWARTZ, M.D., F.A.C.S., St. Louis.

ORTHOPEDIC SURGERY

Friday, 1:30–3:00 p.m., Renaissance Room, Ambassador

Fractures of the Neck of the Femur
Moderator: EDWIN F. CAVE, M.D., F.A.C.S., Boston.
Collaborators: JAMES A. DICKSON, M.D., F.A.C.S., Cleveland; CARROLL B. LARSON, M.D., F.A.C.S., Iowa City; MARCUS J. STEWART, M.D., F.A.C.S., Memphis.

3:15–4:45 p.m., Renaissance Room, Ambassador

Soft Tissue Tumors of the Extremities
Moderator: RALPH K. GHORMLEY, M.D., F.A.C.S., Rochester, Minn.
Collaborators: EDWARD H. SOULE, M.D., Rochester, Minn.; JOHN C. IVINS, M.D., F.A.C.S., Rochester, Minn.; H. HERMAN YOUNG, M.D., F.A.C.S., Rochester, Minn.

PLASTIC SURGERY

Friday, 1:30–3:00 p.m., Ballroom, Ritz Carlton

Problems in Cleft Lip and Cleft Palate Repair
Moderator: BRADFORD CANNON, M.D., F.A.C.S., Boston.
Collaborators: PRESTON C. IVERSON, M.D., F.A.C.S., Philadelphia; W. BRANDON MACOMBER, M.D., F.A.C.S., Albany; ROBERT E. MORAN, M.D., F.A.C.S., Washington, D.C.

3:15–4:45 p.m., Ballroom, Ritz Carlton

Reconstructive Surgery of the Nose
Moderator: FRANK MCDOWELL, M.D., F.A.C.S., St. Louis.
Collaborators: JOHN B. ERICH, M.D., F.A.C.S., Rochester, Minn.; E. HORACE KLABUNDE, M.D., F.A.C.S., San Francisco; THOMAS W. STEVENSON, M.D., F.A.C.S., New York.

THORACIC SURGERY

Friday, 1:30–3:00 p.m., Meeting Room C & D, Convention Hall

Thoracic Surgery in the Aged
Moderator: BRIAN B. BLADES, M.D., F.A.C.S., Washington, D.C.
Collaborators: JOHN H. GIBBON, JR., M.D., F.A.C.S., Philadelphia; EDWARD M. KENT, M.D., Pittsburgh; CHARLES W. THOMPSON, M.D., F.A.C.P., Washington, D.C.

3:15–4:45 p.m., Meeting Room C & D, Convention Hall

New Developments in the Surgery of Heart Disease
Moderator: JULIAN JOHNSON, M.D., F.A.C.S., Philadelphia.
Collaborators: ALFRED BLALOCK, M.D., F.A.C.S., Baltimore; ROBERT E. GROSS, M.D., F.A.C.S., Boston; DWIGHT E. HARKEN, M.D., F.A.C.S., Boston; RICHARD L. VARCO, M.D., F.A.C.S., Minneapolis.

OTOLARYNGOLOGY

Tuesday, 9:00–11:00 a.m., Renaissance Room, Ambassador

Special film session with personal narration.

3:30–5:00 p.m., Renaissance Room, Ambassador

Relationship of Blood Dyscrasias to Otolaryngology Including the Control of Bleeding
Moderator: LOUIS H. CLERF, M.D., F.A.C.S., Philadelphia.
Collaborators: VICTOR C. MCCUAIG, M.D., F.A.C.S., New York; HENRY D. RENTSCHLER, M.D., F.A.C.S., Sayre; LEANDRO M. TOCANTINS, M.D., Philadelphia.

Wednesday, 9:00–10:30 a.m., Renaissance Room, Ambassador

Congenital Diseases of the Larynx—DANIEL C. BAKER, JR., M.D., F.A.C.S., New York.
Borderline Malignant Lesions of the Larynx—F. JOHNSON PUTNEY, M.D., F.A.C.S., Philadelphia.
Carcinoma of the Mouth and Tongue, Including Hemihyoidectomy in the Performance of the Commando Operation—JOEL J. PRESSMAN, M.D., F.A.C.S., Los Angeles.

3:30–5:00 p.m., Renaissance Room, Ambassador

Management of Sinus Disease
Moderator: EDWARD J. WHALEN, M.D., F.A.C.S., Hartford, Conn.
Collaborators: EDWARD H. CAMPBELL, M.D., F.A.C.S., Philadelphia; FRED W. DIXON, M.D., F.A.C.S., Cleveland; I. JEROME HAUSER, M.D., F.A.C.S., Detroit.

Thursday, 9:00–10:30 a.m., Renaissance Room, Ambassador

Nasopharyngeal Fibroma—JOHN B. ERICH, M.D., F.A.C.S., Rochester, Minn.
Cancer of the Nasopharynx—DANIEL MILLER, M.D., F.A.C.S., Boston.
X-Ray Diagnosis of Lesions of the Nasopharynx—RODERICK L. TONDREAU, M.D., Philadelphia.

10:45–12:00 noon, Renaissance Room, Ambassador

Special film session with personal narration.

OPHTHALMOLOGY

Tuesday, 1:00–3:00 p.m., Renaissance Room, Ambassador

Panel Discussion on Surgical Management of Diseases of the Cornea
Moderator: RUDOLF AEBLI, M.D., F.A.C.S., New York.
Collaborators: WILLIAM B. CLARK, M.D., F.A.C.S., New Orleans; HERBERT M. KATZIN, M.D., F.A.C.S., New York; BRENDAN D. LEAHEY, M.D., F.A.C.S., Lowell, Mass.; R. TOWNLEY PATON, M.D., F.A.C.S., New York.

Wednesday, 1:00–3:00 p.m., Renaissance Room, Ambassador

Minor Surgical Problems of the Eye and Adnexae
Moderator: ROBISON D. HARLEY, M.D., F.A.C.S., Atlantic City.
Collaborators: IRVING H. LEOPOLD, M.D., F.A.C.S., Philadelphia; HOMER R. MATHER, JR., M.D., F.A.C.S., Latrobe, Pa.; JOHN M. MCLEAN, M.D., New York.

Thursday, 1:00–3:00 p.m., Renaissance Room, Ambassador

Selection of Operative Technique in Retinal Separation

Moderator: HAROLD G. SCHEIE, M.D., F.A.C.S., Philadelphia.

Collaborators: PAUL A. CHANDLER, M.D., Boston; JOHN W. HENDERSON, M.D., Rochester, Minn.; WILLIAM F. HUGHES, JR., M.D., Chicago.

Tuesday, Wednesday, Thursday, 8:30–10:00 p.m., Renaissance Room

Special film sessions with personal narration.

POSTGRADUATE COURSES

CARDIOVASCULAR SURGERY

JOHN H. GIBBON, JR., M.D., F.A.C.S., Philadelphia, *Chairman*

Monday, 8:30—11:30 a.m., St. Denis Room, Dennis

First half: Portal Hypertension and Bleeding Esophageal Varices.

Second half: Surgical Treatment of Acquired Cardiac Diseases.

Tuesday, 8:30—11:30 a.m.

Congenital Anomalies of the Heart and Great Vessels.

Wednesday 8:30—11:30 a.m.

Cardiac Septal Defects, Transpositions, Hypothermia, and Extracorporeal Blood Circuits.

Thursday, 8:30—11:30 a.m.

Aneurysms and Arteriosclerosis.

NOTE: Participants and additional topics will appear in the official Congress program and the November *Bulletin* of the College.

PREOPERATIVE AND POSTOPERATIVE CARE

JONATHAN E. RHOADS, M.D., F.A.C.S., Philadelphia, *Chairman*

Monday, 8:30—11:30 a.m., Room 20, Convention Hall

Preparation of Patients for Various Operative Procedures

Preanesthetic Medication. JAMES E. ECKENHOFF, M.D., Philadelphia.

Evaluation of the Patient as an Operative Risk. CARL A. MOYER, M.D., F.A.C.S., St. Louis.

Assessment and Replacement of Deficits in Body Water, Electrolytes, and Blood Components. JAMES D. HARDY, M.D., F.A.C.S., Memphis.

Certain Problems of Underweight and Overweight. EDWIN H. ELLISON, M.D., F.A.C.S., Columbus.

Preparation of the Alimentary Tract for Various Operative Procedures. EDGAR J. POTH, M.D., F.A.C.S., Galveston.

Rapid Preparation of Unbalanced Patients for Emergency Operations. FRANCIS D. MOORE, M.D., F.A.C.S., Boston.

Tuesday, 8:30—11:30 a.m.

Special Problems in the Surgical Care of Patients with Biliary Tract Disease

Differential Diagnosis of Infections, Hemolytic and Obstructive Jaundice. JOHN R. NEEFE, M.D., Philadelphia.

Preparation of the Jaundiced Patient for Operative Procedures. STANLEY M. LEVENSON, M.D., Washington, D.C.

The Complications Peculiar to the Biliary Tract and Their Management: Liver Shock; Pancreatic Asthenia; Hypoprothrombinemia; Hepatorenal Syndrome. FRANK GLENN, M.D., F.A.C.S., New York.

Postcholecystectomy Syndrome. W. EMORY BURNETT, M.D., F.A.C.S., Philadelphia.

Wednesday, 8:30—11:30 a.m.

Postoperative Complications, Prophylaxis, and Treatment

Pulmonary. WILLIAM H. MULLER, JR., M.D., F.A.C.S., Los Angeles.

Urinary. REED M. NESBIT, M.D., F.A.C.S., Ann Arbor.
Gastrointestinal. RICHARD WARREN, M.D., F.A.C.S., Brookline.
Wound. PHILIP B. PRICE, M.D., F.A.C.S., Salt Lake City.
Cardiovascular. CHARLES GARDNER CHILD III, M.D., F.A.C.S., Boston.
Neuropsychiatric. WILLIAM. A. HARVEY, M.D., Philadelphia.

Thursday, 8:30—11:30 a.m.

Special Problems in Preoperative and Postoperative Care

The Management of Dumping Syndrome. THOMAS E. MACHELLA, M.D., Philadelphia.
The Management of Anuria. W. J. KOLFF, M.D., Cleveland.
The Management of Peripheral Ischemia. RALPH A. DETERLING, JR., M.D., F.A.C.S., New York.

SURGERY OF THE LOWER ESOPHAGUS, STOMACH AND DUODENUM

REGINALD H. SMITHWICK, M.D., F.A.C.S., Boston, *Chairman*

Monday, 8:30—11:30 a.m., Ballroom, Ritz Carlton

Lesions of the Lower Esophagus

LAMAR SOUTTER, M.D., F.A.C.S., Boston, *Moderator.*

Carcinoma of the Esophagus:

Treatment by Resection and Esophagogastric Anastomosis. JOHN R. PAINE, M.D., F.A.C.S., Buffalo.
Treatment by Resection and Esophagojejunal Anastomosis. WILLIAM F. RIENHOFF, JR., M.D., F.A.C.S., Baltimore.
Combined Treatment by Surgery and Roentgen Therapy. HERBERT D. ADAMS, M.D., F.A.C.S., Boston.

Bleeding Esophageal Varices:

Treatment by Ligation; Technique and Results. GEORGE CRILE, JR., M.D., F.A.C.S., Cleveland.
Treatment by the Use of Balloons and the Pros and Cons of Early Portal Caval Anastomosis. ROBERT R. LINTON, M.D., F.A.C.S., Brookline.

Achalasia:

Pathological Physiology. FRANZ J. INGELFINGER, M.D., Boston.
Indications for and Results of Surgical Treatment. ROBERT H. WYLIE, M.D., F.A.C.S., New York.

Reflux Esophagitis Associated with Hiatus Hernia:

Management in Infants and Children. ORVAR SWENSON, M.D., F.A.C.S., Boston.
Diagnosis and Therapy by Means of the Esophagoscope. EDWIN N. BROYLES, M.D., Baltimore.
Surgical Treatment by Operations Other Than Resection. GUSTAF E. LINDSKOG, M.D., F.A.C.S., New Haven.
The Indications for and Results of Esophagogastric Resection. OWEN H. WANGENSTEEN, M.D., F.A.C.S., Minneapolis.

Tuesday, 8:30—11:30 a.m.

Gastric Neoplasms

HOWARD K. GRAY, M.D., F.A.C.S., Rochester, Minnesota, *Moderator.*
Introductory Remarks, HOWARD K. GRAY, M.D., F.A.C.S., Rochester, Minnesota.

Benign Gastric Neoplasms:

Pathologic Features of Benign Gastric Neoplasms. OSBORNE A. BRINES, M.D., F.C.A.P., Detroit.
Roentgenologic Diagnosis of Benign Gastric Neoplasms. RICHARD SCHATZKI, M.D., Brookline.
Surgery of Benign Gastric Neoplasms. GEORGE T. PACK, M.D., F.A.C.S., New York.

Malignant Gastric Neoplasms:

Cancer of the Stomach and Allied Conditions—Pathologic Features. OSBORNE A. BRINES, M.D., F.C.A.P., Detroit.
Roentgen Manifestations of Malignant Gastric Neoplasms. RICHARD SCHATZKI, M.D., Brookline.
Problems Relating to the Management of Gastric Neoplasms Other Than Carcinoma. I. RIDGEWAY TRIMBLE, M.D., F.A.C.S., Baltimore.
What Constitutes an Adequate Operation for Carcinoma of the Stomach? GEORGE T. PACK, M.D., F.A.C.S., New York.
Palliative Surgical and Medical Procedures for Cancer of the Stomach. I. RIDGEWAY TRIMBLE, M.D., F.A.C.S., Baltimore.

Roentgenologic Therapy. RICHARD SCHATZKI, M.D., Brookline.
Prognosis and End Results. GEORGE T. PACK, M.D., F.A.C.S., New York.

Summary and Question and Answer Period:
All participants.

Wednesday, 8:30—11:30 a.m.

Gastric Ulcer and the Ulcer-Cancer Problem

CLAUDE E. WELCH, M.D., F.A.C.S., Boston, *Moderator.*
The Indications for Surgery in the Therapy of Gastric Ulcer and the Results of Such Therapy. JAMES C. CAIN, M.D., Rochester, Minnesota.

The Differentiation of Benign and Malignant Ulcer:

Studies in Gastric Cytology. WILLIAM A. COOPER, M.D., F.A.C.S., New York.
The Value and Limitations of Endoscopy. EDWARD B. BENEDICT, M.D., F.A.C.S., Boston.
The Value and Limitations of Radiological Examination. RICHARD SCHATZKI, M.D., Brookline.

The Surgical Therapy of Benign and Malignant Gastric Ulcer:

The Selection of the Operation for Gastric Ulcer. RALPH COLP, M.D., F.A.C.S., New York.
The Treatment of the High Gastric Ulcer by Resection. RICHARD H. SWEET, M.D., F.A.C.S., Boston.

Thursday, 8:30—11:30 a.m.

Duodenal Ulcer

HENRY N. HARKINS, M.D., F.A.C.S., Seattle, *Moderator.*
Introductory Remarks. HENRY N. HARKINS, M.D., F.A.C.S., Seattle.
Physiologic Factors in the Production of Duodenal Peptic Ulcer. LESTER R. DRAGSTEDT, M.D., F.A.C.S., Chicago.
Subtotal Gastrectomy as a Surgical Treatment for Duodenal Ulcer.
Billroth II Resection, HENRY K. RANSOM, M.D., F.A.C.S., Ann Arbor.
Billroth I Resection, HENRY N. HARKINS, M.D., F.A.C.S., Seattle.
Longitudinal Tubular Resection, OWEN H. WANGENSTEEN, M.D., F.A.C.S., Minneapolis.
Vagotomy as a Surgical Treatment for Duodenal Ulcer.
With Posterior Gastro-enterostomy. STANLEY O. HOERR, M.D., F.A.C.S., Cleveland.
With Heineke-Mikulicz Pyloroplasty. JOSEPH A. WEINBERG, M.D., F.A.C.S., Long Beach, California.
With Hemigastrectomy. DOUGLAS A. FARMER, M.D., F.A.C.S., Boston.
With Subtotal Gastrectomy. RALPH COLP, M.D., F.A.C.S., New York.
Complications of Procedures Utilized in the Surgical Treatment of Duodenal Ulcer.
Marginal Ulcer. DOUGLAS A. FARMER, M.D., F.A.C.S., Boston.
Dumping Syndrome. HENRY T. RANDALL, M.D., F.A.C.S., New York.
Nutritional Problems. ROBERT M. ZOLLINGER, M.D., F.A.C.S., Columbus.
Pancreatic Injuries. KENNETH W. WARREN, M.D., F.A.C.S., Boston.
Summary and Question and Answer Period—All participants.

DISEASES OF THE LIVER, BILIARY TRACT AND PANCREAS

NATHAN A. WOMACK, M.D., F.A.C.S., Chapel Hill, *Chairman*

Monday, 8:30—11:30 a.m., Rose Room, The Traymore

OLIVER COPE, M.D., F.A.C.S., Boston, *Moderator*
Clinical Aspects of Hepatic Circulation and Hepatic Anomalies. CHARLES GARDNER CHILD, III, M.D., F.A.C.S., Boston.
Liver Dysfunction, Its Recognition and Treatment. I. S. RAVDIN, M.D., F.A.C.S., Philadelphia.
Experimental Aspects of Hepatic Blood Flow and Function. JESSE L. BOLLMAN, M.D., Rochester, Minnesota.
Surgical Therapy of Portal Hypertension. LOUIS M. ROUSSELOT, M.D., F.A.C.S., New York.

Tuesday, 8:30—11:30 a.m.

W. EMORY BURNETT, M.D., F.A.C.S., Philadelphia, *Moderator.*
The Jaundiced Patient. JOHN A. GIUS, M.D., F.A.C.S., Iowa City.
Trauma to the Liver. ROBERT S. SPARKMAN, M.D., F.A.C.S., Dallas.
Abscess of the Liver. ALTON OCHSNER, M.D., F.A.C.S., New Orleans.

Cancer of the Liver and Gallbladder. CONRAD R. LAM, M.D., F.A.C.S., Detroit.
The Methods of Common Bile Duct Repair, WILLIAM P. LONGMIRE, JR., M.D., F.A.C.S., Los Angeles.
The End Results of Common Bile Duct Repair. RICHARD B. CATTELL, M.D., F.A.C.S., Boston.

Wednesday, 8:30—11:30 a.m.

HOWARD A. PATTERSON, M.D., F.A.C.S., New York, *Moderator.*

The Pathogenesis of Cholecystitis. COLIN G. THOMAS, JR., M.D., F.A.C.S., Chapel Hill.
Cholecystography—Then and Now. WARREN H. COLE, M.D., F.A.C.S., Chicago.
The Treatment of Acute Cholecystitis. FRANK GLENN, M.D., F.A.C.S., New York.
Silent Gallstones. HOWARD K. GRAY, M.D., F.A.C.S., Rochester, Minnesota.
The Problem of Common Duct Stones. JOHN R. PAINE, M.D., F.A.C.S., Buffalo.
The Persistence of Symptoms Following Cholecystectomy. FRANK R. PETERSON, M.D., F.A.C.S., Cedar Rapids, Iowa.

Thursday, 8:30—11:30 a.m.

WILLIAM BARCLAY PARSONS, M.D., F.A.C.S., New York, *Moderator.*

Acute Pancreatitis.
Chronic Pancreatitis.
Pancreatic Lithiasis.
The Pathology of Pancreatic Tumors.
Pancreatic Resection for Tumor.
The Metabolic Effects of Pancreatic Resection.

COMBINED INJURIES TO THE EXTREMITIES

HARRISON L. MCLAUGHLIN, M.D., F.A.C.S., and HAROLD A. ZINTEL, M.D., F.A.C.S., New York, *Co-Chairmen*

Monday, 8:30—11:30 a.m., Room 21, Convention Hall

Combined Injuries to the Pelvis and Hip

EARL MILES, M.D., F.A.C.S., Brooklyn, *Moderator.*

Participants:

HARRISON L. MCLAUGHLIN, M.D., F.A.C.S., New York.
FRANCIS D. MOORE, M.D., F.A.C.S., Boston.
E. JEFFERSON BROWDER, M.D., F.A.C.S., Brooklyn.
VICTOR F. MARSHALL, M.D., F.A.C.S., New York.

Tuesday, 8:30—11:30 a.m.

Care of Hand Injuries

HANS MAY, M.D., F.A.C.S., Philadelphia, *Moderator.*

Principles in Primary Repair of Wounds of the Hand. CONDICT W. CUTLER, JR., M.D., F.A.C.S., New York.
Closure of Surface Defects of the Hand. RICHARD S. OAKEY, JR., M.D., F.A.C.S., Philadelphia.
Management of Major Hand Infections. J. EDWARD FLYNN, M.D., F.A.C.S., Boston.
Secondary Tendon Repair. MICHAEL L. MASON, M.D., F.A.C.S., Chicago.
Anatomy of the Hand. ERNEST W. LAMPE, M.D., F.A.C.S., New York.

Wednesday, 8:30—11:30 a.m.

Combined Injuries of the Shoulder and Upper Arm

FREDERICK M. SMITH, M.D., F.A.C.S., New York, *Moderator.*

Participants:

GEORGE J. CURRY, M.D., F.A.C.S., Flint, Michigan.
FRANK H. MAYFIELD, M.D., F.A.C.S., Cincinnati.
JERE W. LORD, JR., M.D., F.A.C.S., New York.
THOMAS W. STEVENSON, M.D., F.A.C.S., New York.

Thursday, 8:30—11:30 a.m.

Combined Injuries of the Knee and Leg

JOHN R. MOORE, M.D., F.A.C.S., Philadelphia, *Moderator.*

Ligamentous Injuries about the Knee, Ankle, and Foot. ARTHUR F. SEIFER, M.D., Philadelphia.

Circulatory Injuries at Knee Level or Below. GEORGE P. ROSEMOND, M.D., F.A.C.S., Philadelphia.
Nerve Injuries at Knee Level or Below. FREDERICK K. MURTAGH, JR., M.D., Philadelphia.
Fractures and Fracture Dislocations Involving Knee and Ankle. JOHN W. LACHMAN, M.D., Philadelphia.
Fractures of the Shaft of the Tibia and Fibula and Bones of the Foot. MATTHEW MISCHINSKI, M.D., and EDWARD RESNICK, M.D., Philadelphia.
Repair of Skin Defects. H. TAYLOR CASWELL, M.D., F.A.C.S., Philadelphia.
Amputations. JOHN T. EALY, M.D., Philadelphia.
General Discussion and Presentation of Problem Cases.

SURGICAL PROCEDURES IN GYNECOLOGY AND OBSTETRICS—INDICATIONS. ANESTHESIA, TECHNIQUE

THADDEUS L. MONTGOMERY, M.D., F.A.C.S., Philadelphia, *Chairman*

Monday, 8:30—11:30 a.m., Ocean Hall, Marlborough-Blenheim

Obstetric Operations and Delivery

THADDEUS L. MONTGOMERY, *Moderator.*

Spontaneous Vaginal Delivery. THADDEUS L. MONTGOMERY, M.D., F.A.C.S., Philadelphia.
Operations of Vaginal Delivery. JOHN E. SAVAGE, M.D., F.A.C.S., Baltimore.
Cesarean Section. MILTON L. MCCALL, M.D., F.A.C.S., New Orleans.

Tuesday, 8:30—11:30 a.m.

Vagino-Plastic Procedures

LAWRENCE R. WHARTON, M.D., Baltimore, *Moderator.*

Surgery in Deficiency of Mullerian Duct Development or Fusion. LAWRENCE R. WHARTON, M.D.
Repair of Fistulae and Complete Laceration and Correction of Incontinence. ANDREW A. MARCHETTI, M.D., F.A.C.S., Washington, D. C.
Vagino-Plastic Correction of Cystocele and Rectocele. JOHN B. MONTGOMERY, M.D., F.A.C.S., Philadelphia.

Wednesday, 8:30—11:30 a.m.

Hysterectomy, Myomectomy

THADDEUS L. MONTGOMERY, *Moderator.*

Abdominal Myomectomy, Supracervical Hysterectomy, Panhysterectomy. RICHARD TELINDE, M.D. Baltimore.
Vaginal Hysterectomy. EUGENE A. EDWARDS, M.D., F.A.C.S., Chicago.
The Wertheim Operation. HOWARD ULFELDER, M.D., F.A.C.S., Boston.

Thursday, 8:30—11:30 a.m.

Tubo-Ovarian Surgery

CLYDE L. RANDALL, M.D., Buffalo, *Moderator.*

Disposal of Tubes and Ovaries in Chronic Pelvic Infection. HENRY C. FALK, M.D., F.A.C.S., New York.
Surgery in Ovarian and Pelvic Endometriosis. CLAYTON T. BEECHAM, M.D., F.A.C.S., Philadelphia.
Tubal Operations in Sterility. MARIO A. CASTALLO, M.D., F.A.C.S., Philadelphia.
Surgery of Malignant Ovarian Disease. CLYDE L. RANDALL, M.D., Buffalo.

SURGICAL ASPECTS OF PULMONARY DISEASE

RICHARD H. OVERHOLT, M.D., F.A.C.S., Brookline, *Chairman*

Monday, 8:30—11:30 a.m., 22 Club, Ambassador

Preoperative Preparation, Anesthesia and Postoperative Management

HERBERT C. MAIER, M.D., F.A.C.S., New York, *Moderator.*

Participants:

JOHN C. JONES, M.D., F.A.C.S., Los Angeles.
EMANUEL M. PAPPER, M.D., New York.
JOHN W. STRIEDER, M.D., F.A.C.S., Brookline.

Tuesday, 8:30—11:30 a.m.

Surgical Management of Pulmonary Tuberculosis

ROBERT R. SHAW, M.D., F.A.C.S., Dallas, *Moderator.*

Participants:

J. MAXWELL CHAMBERLAIN, M.D., F.A.C.S., New York.
WINTHROP N. DAVEY, M.D., Ann Arbor.
JAMES D. MURPHY, M.D., F.A.C.S., Oteen, North Carolina.
NORMAN J. WILSON, M.D., F.A.C.S., Brookline.

Wednesday, 8:30—11:30 a.m.

Management of Diseases Other Than Tuberculosis or Neoplasm

DUANE CARR, M.D., F.A.C.S., Memphis, *Moderator.*

Bronchiectasis. FRANCIS M. WOODS, M.D., F.A.C.S., Brookline.
Cystic Disease. HERBERT C. MAIER, M.D., F.A.C.S., New York.
Spontaneous Pneumothorax. RICHARD H. MEADE, JR., M.D., F.A.C.S., Grand Rapids.
Trauma. THOMAS H. BURFORD, M.D., F.A.C.S., St. Louis.
Surgical Fungus Diseases. FELIX A. HUGHES, JR., M.D., F.A.C.S., Memphis.

Thursday, 8:30—11:30 a.m.

Surgical Problems of Pulmonary Neoplasms

RICHARD H. OVERHOLT, M.D., F.A.C.S., Brookline, *Moderator.*

X-Ray Aspects. JOSEPH H. MARKS, M.D., Boston.
Isotopes. BRADLEY E. COPELAND, M.D., Boston.
Use of Deep X-Ray Therapy. WILLIAM A. MEISSNER, M.D., Boston.
Surgical Aspects. JOHN L. POOL, M.D., F.A.C.S., New York.

LOWER EXTREMITY AMPUTATIONS AND PROSTHESES

HARRY D. MORRIS, M.D., F.A.C.S., New Orleans, *Chairman*

Monday through Thursday, 8:30—11:30 a.m., Venetian Room, Ambassador

This Postgraduate Course will cover the following topics:

Amputations About the Foot and Ankle, Including Syme Amputation. ERNEST A. BRAV, Col. M.C., U.S.A., F.A.C.S., Washington, D.C.

Below and Above Knee Amputations—Indications, Technique, Prosthetic Fitting. CLINTON L. COMPERE, M.D., F.A.C.S., Chicago, and CHARLES O. BECHTOL, M.D., F.A.C.S., New Haven

Special Amputation Problems of Surgical Technique and Fitting in Children. CHARLES N. FRANTZ, M.D., F.A.C.S., Grand Rapids.

The Open Amputation—Indications, Technique, After Care, and Subsequent Plastic Revision. HARRY D. MORRIS, M.D., F.A.C.S. New Orleans.

Special Amputation Problems in Patients with Peripheral Vascular Disease. LELAND S. MCKITTRICK, M.D., F.A.C.S., Brookline.

Rehabilitation of the Lower Extremity Amputee. ROY R. SCHUBERT, M.D., F.A.C.S., Paterson, N. J.

NOTE: Participants and additional topics will appear in the official Congress program and the November *Bulletin* of the College.

SYMPOSIUM ON TRAUMA

Tuesday, 2:00–5:00 p.m., American Room, The Traymore

R. ARNOLD GRISWOLD, M.D., F.A.C.S., Louisville, Chairman, Committee on Trauma, *Presiding.*

Prevention of Injuries in Automobile Accidents. HORACE E. CAMPBELL, M.D., F.A.C.S., Denver, and COL. DON S. WENGER, M.D., F.A.C.S., Washington, D.C.

Painful Posttraumatic Dystrophies. FRANK H. MAYFIELD, M.D., F.A.C.S., Cincinnati.

Fractures in Children. CHARLES F. WOOD, M.D., F.A.C.S., Louisville.

Tetanus Prophylaxis—The Duration of Protection from Active Immunization. EDWARD S. STAFFORD, M.D., F.A.C.S., Baltimore.

Conservatism in the Treatment of Fractures. HAROLD A. SOFIELD, M.D., F.A.C.S., Chicago.

SYMPOSIUM ON CANCER

Wednesday, 2:00–5:00 p.m., American Room, The Traymore

DANELY P. SLAUGHTER, M.D., F.A.C.S., Chicago, Acting Chairman, Committee on Cancer, American College of Surgeons, *Presiding.*

Carcinoma of the Lung: a Health Menace. ALTON OCHSNER, M.D., F.A.C.S., New Orleans.

Results of Surgical Treatment of Breast Cancer at the Johns Hopkins Hospital. EDWARD F. LEWISON, M.D., F.A.C.S., Baltimore.

Treatment of Cancer of the Cervix. HOWARD ULFELDER, M.D., F.A.C.S., Boston.

Tumors of the Peripheral Nervous System. ARTHUR PURDY STOUT, M.D., New York.

Brain Tumors. PAUL C. BUCY, M.D., F.A.C.S., Chicago.

SYMPOSIUM ON GRADUATE TRAINING IN SURGERY AND THE SURGICAL SPECIALTIES

Thursday, 1:30–3:00 p.m., Meeting Room A, Convention Hall

MOTION PICTURE SYMPOSIUM ON SPECTACULAR SURGICAL PROBLEMS

Thursday, 8:30–10:00 p.m., American Room, The Traymore

CHARLES. W MAYO, M.D., F.A.C.S., Rochester, Minn., *Presiding Officer.*

FORUM ON FUNDAMENTAL SURGICAL PROBLEMS

Heart

Monday, 9:00 a.m.—12:00 noon

Experience with the Bjork-Crafoord Operation for Closure of Atrial Septal Defect. JAMES L. SOUTHWORTH and C. HARWELL DABBS, Knoxville.

The Implantation of a Vascularized Graft in the Chambers of the Heart; an Experimental Approach to the Correction of Valvular Insufficiency. WILLIAM W. L. GLENN and L. NEWTON TURK, New Haven.

Experimental Surgery of the Mitral Valve Under Direct Vision Using Hypothermia. NORMAN E. SHUMWAY and F. JOHN LEWIS, Minneapolis.

Use of the Right Auricle as a Pump for the Pulmonary Circuit. HERBERT E. WARDEN, RICHARD A. DEWALL, and RICHARD L. VARCO, Minneapolis.

Experimental Closure of Interventricular Septal Defects and Further Physiologic Studies on Controlled Cross Circulation. HERBERT E. WARDEN, MORLEY COHEN, RICHARD A. DEWALL, EARL A. SCHULTZ, JOSEPH J. BUCKLEY, RAYMOND C. READ, C. WALTON LILLEHEI, Minneapolis.

A Parabiotic Blood Pump. LESTER BLUM, SAMUEL H. MEGIBOW, and WILLIAM M. NELSON, New York.

A New Method for the Drainage of Blood from the Open Heart During Total By-Pass of the Heart and Lungs. JAMES A. HELMSWORTH, LELAND C. CLARK, JR., SAMUEL KAPLAN, and CLYNN FORD, Cincinnati.

Experimental Exposure of the Aortic Valve; Laboratory Studies and a Clinical Trial. GEORGE H. A. CLOWES, JR., and WILLIAM E. NEVILLE, Cleveland.

Hemodynamic Effects of Experimental Drainage of Pulmonary Veins to Right Atrium. D. E. BOWES, H. J. C. SWAN, and J. W. KIRKLIN, Rochester, Minnesota.

Cinematographic Demonstration of Valvular Disorders of the Heart. CHARLES V. MECKSTROTH and KARL P. KLASSEN, Columbus, Ohio.

The Simultaneous Recording of Blood Pressures in the Left Heart and Aorta Before and After Mitral Surgery. AARON HIMMELSTEIN, ALVIN J. GORDON, EUGENE BRAUNWALD, RICHARD P. LASSER, and MARK M. RAVITCH, New York.

Plication of the Annulus in the Correction of Mitral Valvular Insufficiency. ELLIOTT S. HURWITT, PAUL W. HOFFERT, and RUTHVEN FERREIRA, New York.

Ciné Radiographic Studies of Retrograde Coronary Flow. OSLER A. ABBOTT, H. S. WEEMS, FRANK MORGAN, and WILLIAM E. VANFLEIT, Emory University, Georgia.

Metabolism

Monday, 9:00 a.m.—12:00 noon

Amino Acids and Amino Conjugates in Seriously Wounded Soldiers. HYMAN ROSEN and STANLEY M. LEVENSON, Washington.

The Effect of Abdominal Operations upon the Serum Amylase and Serum Lipase. DWIGHT J. HOTCHKISS, JR., WILLIAM T. FITTS, JR., and OTTO ROSENTHAL, Philadelphia.

Metabolic Alterations in Surgical Patients—V, Cause and Management of Hyperchloremic Acidosis Following Ureterosigmoidostomy. LESTER PERSKY, HARVEY KRIEGER, STANLEY LEVEY, and WILLIAM E. ABBOTT, Cleveland.

Metabolic Alterations in Surgical Patients—VI, The Effect on Weight and Nitrogen Balance of Providing Varying Caloric Intakes by Intravenous Carbohydrate, Fat, and Amino Acids in Gastrectomized Patients. WILLIAM E. ABBOTT, JOHN H. DAVIS, JERRELL W. BENSON, HARVEY KRIEGER and STANLEY LEVEY, Cleveland.

The Effect of Parathyroid Hormone upon Serum Levels and Urinary Excretion of Magnesium. BROOKE ROBERTS, JOHN J. MURPHY, and OTTO ROSENTHAL, Philadelphia.

A Rapid Method for the Calculation of the Extracellular Space. JOHN F. PRUDDEN and MELVIN S. SCHWARTZ, Fort Sam Houston.

The Influence of Protein Level on the Volume Expansion and Maintenance Given by Dextran. WILLIAM METCALF and LOUIS M. ROUSSELOT, New York.

The Renal Clearance of Plasma Expanders. WILLIAM METCALF, LOUIS M. ROUSSELOT, and F. E. GILBERTSON, New York.

Total Body Potassium as Measured by Radioactive Potassium (K^{42}). GEORGE C. HENEGAR, Oakland.

The Use of Stable Rubidium for Measurement of Total Exchangeable Body Potassium. JULIAN S. ANSELL and BERNARD ZIMMERMANN, Minneapolis.

The Use of Erythrocytes Labelled with Radioactive Chromium-51. TIMOTHY R. TALBOT, JR., MARY SAX, and ALICE CARY, Philadelphia.

Blood Circulation. Vital Staining of Lymphatics.

Monday, 2:00—5:00 p.m.

Observations on the Venous Flow Rate in the Lower Extremities; Effect of Compression Bandages and Elevations. PAUL F. PAULSEN, OSCAR CREECH, JR., and MICHAEL E. DEBAKEY, Houston.

The Effect of Subtotal Adrenalectomy upon the Development of Ascites in Chronic Heart Failure. JOSEPH L. SPRAFKA, DONALD W. HANNON, and IVAN D. BARONOFSKY, Minneapolis.

The Renal Factor in the Hypertension of Experimental Coarctation of the Aorta. R. C. HARRISON and J. D. M. ALTON, Edmonton, Alberta.

A Quantitative Experimental Comparison of the Effects of Severe Hypercapnea on the Brain and Heart. AMOS L. HOPKINS, JORGE ANZOLAS, and GEORGE H. A. CLOWES, JR., Cleveland.

The Augmentation of Peripheral Arterial Blood Flow by the Use of a Valve. ADRIAN KANTROWITZ and ALAN LERRICK, New York.

Polarigraphic Studies on Circulation in the Dog. CHARLES C. WOLFERTH, JR., ANDREW BOYD, JR., and WILLIAM T. FITTS, JR., Philadelphia.

Measurement of Ambulatory Venous Pressure in the Lower Extremity. KARL A. LOFGREN, Rochester, Minnesota.

The Effect of Prior Asphyxia and Recovery on the Pulmonary Blood Volume Response to Hemorrhage. BEN J. WILSON, ALLEN REID, and M. J. FOGELMAN, Dallas.

Vital Staining of Lymphatics During Surgery. LAWRENCE H. STRUG, WILLIAM LEON, and ISIDORE COHN, JR., New Orleans.

An Experimental Evaluation of Regional Heparinization. DAVID A. OHLWILER and EARLE B. MAHONEY, Rochester, New York.

A Comparison of Thoracolumbar Sympathectomy and Bilateral Adrenalectomy-Sympathectomy in the Treatment of Essential Hypertension. J. A. MACKIE and HAROLD A. ZINTEL, Philadelphia.

The Experimental Use of Negative Electrical Fields to Delay and Prevent Intravascular Thrombosis. P. N. SAWYER and B. DEUTCH, Philadelphia.

Urology

Monday, 2:00—5:00 p.m.

Early Bladder Dysfunction in Poliomyelitis. JAMES PIERCE and HANS H. ZINSSER, Los Angeles.

Biocolloids of Urine in Health and in Calculous Disease. WILLIAM H. BOYCE, FRED K. GARVEY, and CHARLES M. NORFLEET, JR., Winston-Salem.

Urinary Hormone Levels Before and After Castration and Adrenalectomy. J. H. HARRISON, C. B. LEMAN, and J. C. LAIDLAW, Boston.

The Investigation of Possible Mechanisms for Water and Electrolyte Imbalance Following Relief of Prostatic Obstruction. C. G. VIVION, BEN EISEMAN, and J. M. VIVIAN, Denver.

Ureteral Regeneration; Contracture Vs. Hyperplasia of Smooth Muscle. RUDOLPH O. F. OPPENHEIMER and FRANK HINMAN, JR., San Francisco.

The Fate of Autogenous Arterial Grafts Embedded in Submucosal Intestinal Tunnels As Applied to the Bridging of Ureteral Defects. CLARENCE J. SCHEIN, ARNOLD R. SANDERS, and ELLIOTT S. HURWITT, New York.

A Study of the Electrical Activity of Intact and Partially Mobilized Human Ureters. HARVEY R. BUTCHER, JR., and WILLIAM SLEATOR, JR., St. Louis.

Radioactive Isotopes in the Treatment of Inoperable Urological Tumors. VINCENT MOORE, Los Angeles.

Free Grafts of Skin to Resurface the Urinary Bladder. JOHN W. DRAPER and RICHARD B. STARK, New York.

The Use of Seromuscular Grafts in Bladder Reconstruction. WILLIAM C. SHOEMAKER, PAUL J. GROTZINGER HORACE D. MARUCCI, ALEX W. ULIN, and WILLIAM L. MARTIN, Philadelphia.

Burns

Monday, 2:00—5:00 p.m.

An Evaluation of the Relative Importance of Partial Thickness to Full Thickness Burn. HARRY S. SOROFF, MELVIN S. SCHWARTZ, N. CARL-FREDRIK LIEDBERG, JERROLD M. BECKER, and CURTIS P. ARTZ, Fort Sam Houston.

Early Red Cell Deficit After Burn Injury; a Preliminary Report. STEFFEN BIRKELAND, Richmond.

The Successful Use of Dextran in the Treatment and Prevention of Shock in the Burned Patient. EVERETT I. EVANS and MARY M. MARTIN, Columbus, Ohio.

Quantitative Histochemistry of Burned and Normal Skin. FALLS B. HERSHEY, St. Louis.

Lymphatic Lipid Alterations in Thermal Injury; an Experimental Study. J. THOMAS PAYNE and KATHRYN KRAUEL, Seattle.

The Role of Epinephrine in Hyperkalemia of Acute Burns. CLARKE L. HENRY, Fort Sam Houston.

The Aminoaciduria of Trauma. GEORGE L. NARDI, Boston.

The Effect of Levarterenol on Renal Blood Flow in Dogs Subjected to Hemorrhagic Shock. JOHN H. FOSTER, HAROLD A. COLLINS, and H. WILLIAM SCOTT, Jr., Nashville.

Renal Functional Response to Norepinephrine in Shock. GEORGE C. MORRIS, JR., H. LISTON BEAZLEY, and JOHN H. MOYER, Houston.

Experimental Studies on Parenterally Administered Trypsin; its inefficacy as a Thrombolitic Agent. ERIC G. HARDY, GEORGE C. MORRIS, JR., and MICHAEL E. DEBAKEY, Houston.

Blood, Extracellular Fluid and Total Body Water Volume Relationships in the Early Stages of Severe Burns. M. J. FOGELMAN and BEN J. WILSON, Dallas.

Comparison of the Volumes of Distribution of Sucrose and Sodium Thiosulfate as an Estimate of Extracellular Fluid Volume in Burned Humans. JERRY A. STIRMAN, J. F. PRUDDEN, and KENDALL YOUNG, Fort Sam Houston.

Further Observations on the Use of Proteolytic Enzymes in the Removal of the Burn Eschar. LOUIS M. ROUSSELOT and JAMES F. CONNELL, JR., New York.

Vascular Grafts

Tuesday, 9:00 a.m.—12:00 noon

The Use of Heterogenous Vein and Artery Grafts Supported by a Plastic Sponge. JOHN H. MORTON and EARLE B. MAHONEY, Rochester, New York.

Plastic Venous Prostheses. RICHARD H. EGDAHL, D. M. HUME, and H. A. SCHLANG, Bethesda.

The Use of Cloth Prostheses in the Restoration of Blood Vessel Continuity. JOHN L. MADDEN and WILLIAM J. MCCANN, JR., New York.

Comparison of Fates of Orlon Mesh Prosthetic Replacement of Thoracic Aorta and Aortic Bifurcation. SIGMUND A. WESOLOWSKI and LESTER R. SAUVAGE, Washington.

The Use of Braided Plastic-Coated Nylon Tubes for Arterial Restitution by End-to-End Suture Method. MILTON M. SELF, DENTON A. COOLEY, MICHAEL E. DEBAKEY, and OSCAR CREECH, JR., Houston.

Homologous Grafts of the Abdominal Aorta Including the Renal Arteries in Dogs. C. R. BOWERS, D. GOLD, and JOHN A. SCHILLING, Randolph Field.

Observations on the Natural History of Renal Homotransplants in Dogs. J. E. MURRAY, S. LAND, and B. F. MILLER, Boston.

The Sterilization of Human Arterial Homografts with Beta-Propiolactone. Experimental and Clinical Observations. D. EMERICK SZILAGYI, PAUL R. OVERHULSE, CLAIBOURNE P. SHONNARD, and G. A. LOGRIPPO, Detroit.

Chemical Preservation of Vascular Grafts; Effects on Graft Complications. HENRY N. HARKINS, RALPH K. ZECH, T. LLOYD FLETCHER, CHARLES A. GRIFFITH, and LLOYD M. NYHUS, Seattle.

The Development of Experimental Aneurysms in Lyophilized Arterial Heterografts. LEON J. TUNE and J. CUTHBERT OWENS, Denver.

The Importance of Elastic Lamellae in Aortic Grafts and a Technique for the Experimental Production of Aortic Aneurysms. WILLIAM H. SEWELL, WILLIAM H. BATCHELOR, and DOUGLAS R. KOTH, Bethesda.

The Use of Cobalt^{60} As a Sterilizing Agent for Aortic Homografts—I, Effect of Gamma-Ray Irradiation Upon the Structural Integrity of the Graft. JACK A. MACRIS, HERBERT E. SLOAN, and JOHN E. OREBAUGH, Ann Arbor.

Anesthesia and Postoperative Problems

Tuesday, 9:00 a.m.—12:00 noon

The Effects of Narcotics upon the Respiratory Response to Carbon Dioxide in Man. JAMES ECKENHOFF, M. HELRICH, and M. J. D. HEGE, Philadelphia.

The Effect of Surgical Positions on Respiration. JOHN R. JONES and JAY JACOBY, Columbus, Ohio.

The Effect of Unilateral Rebreathing of Low Oxygen Gas Mixtures upon the Pulmonary Blood Flow in Man. WILLIAM S. BLAKEMORE, E. CARLENS, and S. BJORKMAN, Stockholm, Sweden.

Factors Effecting Contralateral Ventilation During Unilateral Atelectasis. W. ANDREW DALE and HERMANN RAHN, Rochester, New York.

Bronchospasm Due to Increased Carbon Dioxide in Inspired Air; a Vagal Reflex. RICHARD M. PETERS, Chapel Hill.

An Evaluation of Antimetic Drugs in the Control of Postoperative Nausea and Vomiting. EDWARD P. DIDIER, TIMOTHY G. BARILE, HARVEY C. SLOCUM, VERNER V. LINDGREN, Washington, and ELTON L. MCCAWLEY, Portland, Oregon.

Use of the Recording Oximeter as a Means of Evaluation of Pulmonary Reserve. WILLIAM E. ADAMS, J. F. PERKINS, JR., MIGUEL CASTELLANOS, ADOLFO FLORES, and RALPH F. CARLSON, Chicago.

The Effect on the Central Nervous System of Interrupted Circulation During Refrigeration Anesthesia. JAMES R. WILLIAMS, MATHEW PRESTI, JOSEPH J. CARROLL, JOHN A. GARVIN, RAYMOND A. CLASEN, and EDWARD J. BEATTIE, JR., Chicago.

Observations on Prolonged Hypothermia in the Dog. BERNARD FISHER, JOHN HAPPEL, CLEM RUSS, and PAUL PRENDERGAST, Pittsburgh.

Studies of the Cerebral Circulation and Metabolism During Acute Drug-Induced Hypotension. HRANT H. STONE, THOMAS N. MACKRELL, and RICHARD L. WECHSLER, Philadelphia.

Evaluation of a Standard Tilt Test for Estimation of Blood Volume Deficiency. CURTIS P. ARTZ, Fort Sam Houston.

Evaluation of Blood Loss From a Standardized Wound After Dextran. ALVIN W. BROWNELL, CURTIS P. ARTZ, and YOSHIO SAKO, Fort Sam Houston.

Cancer

Tuesday, 9:00 a.m.—12:00 noon

A Lymphatic Function Test. DAVID MCJU, ARTHUR BLAKEMORE, and THOMAS W. STEVENSON, New York.

The Use of Radiogold in Studying the Lymphatic Dissemination of Cancer. C. G. THOMAS, JR., Chapel Hill.

Fluorescence of Human Lymphatic and Cancer Tissues Following High Doses of Intravenous Hematoporphyrin. D. S. RUSMUSSEN-TAXDAL, GRANT E. WARD, and FRANK H. J. FIGGE, Baltimore.

The Use of Dietary Deficiencies to Influence the Action of Methycholanthrene upon the Stomach of Mice. CLAUDE R. HITCHCOCK, Minneapolis.

An Anti-Tumor Factor in the Blood of Tumor Immune Rats. ROBERT SCHREK and FREDERICK W. PRESTON, Chicago.

Serial Transplantation of Human Neoplasms in Cortisone-Treated Hamsters. W. BRADFORD PATTERSON, Boston.

Effect of Estrogen and Testosterone on Rate of Nucleic Acid Synthesis in Mouse Mammary Carcinoma. L. PHILIPPE ALLEN, Quebec City and SOMERS H. STURGIS, Boston.

Combination Chemotherapy of Cancer Based upon Quantitative Biochemical Differences. DANIEL M. SHAPIRO, New York.

Isotope Therapy for Carcinoma of the Pancreas. PAUL V. HARPER, Chicago.

Antibodies to Cancer in Patients. JOHN B. GRAHAM and RUTH M. GRAHAM, Boston.

Incidence of Cancer in Thyroid Glands Removed at 1,000 Consecutive Routine Necropsies. J. D. MORTENSEN, W. A. BENNETT, and L. B. WOOLNER, Rochester, Minnesota.

Radiochromium-Labeled Erythrocytes for the Detection of Gastrointestinal Hemorrhage. CHARLES A. OWEN, JR., JESSE L. BOLLMAN, JOHN H. GRINDLAY, and MILTON COOPER, Rochester, Minnesota.

Pancreas

Tuesday, 2:00—5:00 p.m.

The Turnover of Plasma Proteins in States of Liver Injury, Hemorrhage, and Dietary Depletion. ROBERT E. MADDEN, Chicago.

Response of Animals with Biliary Fistula, Bile Duct Occlusion, or Chloroform Intoxication to Parenteral Fat Feeding. STEWART M. SCOTT and HARRY M. VARS, Philadelphia.

Fluorescein Injection into Extrahepatic Biliary Ducts for Differential Diagnosis of Obstructive and Nonobstructive Jaundice. JOSEPH K. NARAT, JOSEPH P. CANGELOSI, and JOHN V. BELMONTE, Chicago.

Serum Mucoprotein Level as an Aid to Differential Diagnosis in Jaundice Patients. EDWIN H. ELLISON, RICHARD O. MOORE, JAMES R. LLOYD, and ROBERT M. ZOLLINGER, Columbus, Ohio.

Primary Reconstruction of the Common Bile Duct Without the Use of Stents. WILLIAM J. MCCANN, JR., and JOHN L. MADDEN, New York.

Blood Volume Deficits in Pancreatitis. LUTHER M. KEITH, JR., and ROBERT N. WATMAN, Columbus, Ohio.

The Mechanism of Benefit Derived from Concentrated Human Serum Albumin in Experimental Acute Pancreatitis. DAN W. ELLIOTT, Columbus, Ohio.

Studies on Pancreatitis—IV, the Ischemic Origin of Experimental Hemorrhagic Pancreatic Necrosis. ALAN THAL, Minneapolis.

Experimental Hemorrhagic Pancreatitis—I, a Method of Production of Noninfected Lethal Hemorrhagic Pancreatitis. M. HARA, J. C. BABER, and P. H. MILLAR, JR., Little Rock.

Studies of Pituitary Factors Affecting the Pancreatic Insular Tissue. KANWAL K. KAPUR, STANLEY C. SKORYNA, and DONALD R. WEBSTER, Montreal.

An Experimental Study of Retrograde Pancreatico-Jejunostomy. JOSEPH A. BONTA, Columbus, Ohio.

Inhibition of Human Pancreatic Secretion by Diamox (Carbonic Anhydrase Inhibitor) Therapeutic Implications in Acute Pancreatitis. DAVID A. DREILING and HENRY JANOWITZ, New York.

Heart and Blood Vessels

Tuesday, 2:00—5:00 p.m.

A Study of Patent Ductus Type Shunts in the Dog Using a New Technique for Measuring Blood Flow. DONALD J. FERGUSON, FLETCHER A. MILLER, and RICHARD L. VARCO, Minneapolis.

Surgical Correction of Transposition of the Great Vessels. HAROLD M. ALBERT, New Orleans.

A Study of the Amount of Blood and Oxygen Delivered to the Myocardium Through the Implanted Internal Mammary Artery. WILLIAM K. BULLER and ARTHUR M. VINEBERG, Montreal.

Experimental Evaluation of an External Shunt for By-Passing the Thoracic Aorta. RALPH D. ALLEY, WILLIAM H. SEWELL, PAUL F. FORMEL, ALLAN STRANAHAN, HARVEY W. KAUSEL, DOUGLAS R. KOTH, Albany and Bethesda.

The Mechanism of Death from Thoracic Aortic Occlusion. W. STERLING EDWARDS, Birmingham, Alabama.

Production of Heart Block in Dogs, Under Direct Vision. MANSUR TAUFIC, FOUAD A. BASHOUR, and F. JOHN LEWIS, Minneapolis.

An Evaluation of the Use of an Electrical Pacemaker to Maintain the Function of the Heart of the Hypothermic Dog. ROBERT H. DERIEMER, RICHARD WEXLER, H. BRODIE STEPHENS, and ROBERT DUNBAR, San Francisco.

The Effect of Carbon Dioxide on Heart-Block and Ventricular Fibrillation During Hypothermia in Rats and Dogs. SUAD A. NIAZI and F. JOHN LEWIS, Minneapolis.

Defibrillation of the Ventricles Under Hypothermic Conditions. C. K. KIRBY, J. M. JENSEN and J. JOHNSON, Philadelphia.

Resumption of Heartbeat in Dogs After Standstill at Low Temperatures. SUAD A. NIAZI and F. JOHN LEWIS, Minneapolis.

The Effect of Total Adrenalectomy Upon Cardiac Output in Dogs with Large Chronic Arteriovenous Fistulae. MITCHELL W. SPELLMAN, Washington, GABRIEL G. NAHAS and C. WALTON LILLEHEI, Minneapolis.

The Effect of Hypothyroidism and Hyperthyroidism on the Susceptibility of Dogs with Arteriovenous Fistulas to Bacterial Endocarditis. RAYMOND C. READ and C. WALTON LILLEHEI, Minneapolis.

Gynecology and Obstetrics

Tuesday, 2:00—5:00 p.m.

Gonadotrophin Titers in Disturbed Pregnancies. EDWARD H. HON and JOHN MCLEAN MORRIS, New Haven.

The Impact of Position on Renal Function in the Near-Term Pregnant Woman. JACK A. PRITCHARD and ALLAN C. BARNES, Cleveland.

Red Cell Survival in Normal Pregnancy and in Toxemia of Pregnancy. LOUIS LOWENSTEIN and ROBERT EDINGTON, Montreal.

Measurements of the Sodium Retaining Factor in the Urine of Women with Eclamptogenic Toxemias. ALLAN C. BARNES, Cleveland.

Quantitative Estimations of Endometrial Glycogen Using the Anthrone Method. H. W. PAYNE and J. P. A. LATOUR, Montreal.

Peripheral Utilization of Glucose in Pregnancy—II, Acute Toxemia. RICHARD L. BURT, Winston-Salem.

Maternal Blood and Breast Milk Estimation Following the Administration of Chloral Hydrate During the Puerperium. J. BERNARD BERNSTINE, RICHARD L. BERNSTINE, and ARTHUR E. MEYER, Philadelphia.

The Use of the Colposcope in the Detection of Cervical Carcinoma. LEWIS C. SCHEFFEY, WARREN R. LANG, and GABRIEL TATARIAN, Philadelphia.

The Preoperative and Operative Blood Volume Status in Gynecological Surgery. MYRON BUCHMAN, New York.

The Curability of Regional Metastases by Irradiation or Surgery in Cancer of the Uterine Cervix. JOHN B. GRAHAM and RUTH M. GRAHAM, Boston.

Lung. Wounds and Infection

Wednesday, 9:00 a.m.—12:00 noon

Experimental Production of Pulmonary Hyaline Membrane. LEONARD E. LAUFE and STUART S. STEVENSON, Pittsburgh.

The Mechanical Elimination of Respiratory Acidosis During "Open" Thoracic Procedures. WILLIAM H. FALOR, T. R. KELLY, and W. REYNOLDS, Akron.

Effect of Simulated Altitude and Explosive Decompression on Dogs with Bilateral Partial Pulmonary Resection. JOHN A. SCHILLING, RODNEY B. HARVEY, and BRUNO BALKE, Randolph Field.

Experimental Principles of Repair of Complete Tracheal Defects. H. MASON MORFIT, ADRIAN J. NEERKEN, ARTHUR E. PREVEDEL, and EDWARD B. LIDDLE, Denver.

Flexible Plastic Casts of the Tracheobronchial Tree and Pulmonary Vessels. CHARLES V. MECKSTROTH and KARL P. KLASSEN, Columbus, Ohio.

Studies on Pulmonary Embolism Utilizing the Method of Controlled Unilateral Pulmonary Artery Occlusion—I, Effect of Distal Injection of Histamine and 5-Hydroxy-Tryptamine. PAUL NEMIR, H. H. STONE, T. N. MACKRELL, and HERBERT R. HAWTHORNE, Philadelphia.

Relationship Between Pulmonary Embolism and Pulmonary Infarction; Experimental Study. H. DAVID ROACH and HAROLD LAUFMAN, Chicago.

Effect of Decreased Body Temperature on Liver Function and Splanchnic Blood Flow in Dogs. E. BRUCE HALLETT, Rochester, New York.

Studies of Growth Hormone by Means of Liver Perfusion. JOHN F. PRUDDEN, M. KENDALL YOUNG, and JERRY A. STIRMAN, Fort Sam Houston.

An Outbreak of Wound Infections Due to Antibiotic Resistant Staphylococcus Aureus. JEROME J. LANDY, ISABEL HAVENS, JAMES S. CLARKE, ROSS S. BENHAM, Chicago.

Effect of Increased Fibrinolysis on the Tensile Strength of Wounds in the Early Latent Phase. H. DAVID ROACH and HAROLD LAUFMAN, Chicago.

A New Test for Proteolytic and Antiproteolytic Activity Determination. KAREL B. ABSOLON, Minneapolis.

Studies on Intravascular Proteolysis Concerned with the Experimental Production of Lower Nephron Nephrosis. A. D. MASON, C. BARBER MUELLER, and D. G. STOUT, St. Louis.

Gastrointestinal Tract

Wednesday, 9:00 a.m.—12:00 noon

The Role of the Pyloric Antrum in Experimentally Induced Peptic Ulceration in Dogs. DAVID STATE, ALFRED KATZ, ROBERT S. KAPLAN, BERNARD HERMAN, LEON MORGENSTERN, and IRVING A. KNIGHT, Los Angeles.

The Relative Effects of Different Gastric Drainage Procedures on the Hormonal Phase of Gastric Secretion. RALPH K. ZECH, LLOYD M. NYHUS, HORACE G. MOORE, JR., LESTER R. SAUVAGE, CHARLES A. GRIFFITH, and HENRY N. HARKINS, Seattle.

Effects of ACTH on Gastric Secretion. PAUL GERITY, J. A. CAMILLERI, and MARK A. HAYES, New Haven.

Further Studies of Experimental Gastric and Duodenal Ulcers in Dogs. EDWARD B. C. KEEFER, DANIEL M. HAYS, KIRBY A. MARTIN, JOHN M. BEAL, and FRANK GLENN, New York.

The Effect of Migration of the Stomach to the Lower Jejunum with the Presentation of Vagal Innervation. W. D. KELLY and OWEN H. WANGENSTEEN, Minneapolis.

Transplantation of the Pyloric Antrum to the Colon; Effect on Canine Gastric Secretion. JOHN BOTTI, GEORGE A. HALLENBECK, and JOHN H. GRINDLAY, Rochester, Minnesota.

The Interposed Jejunal Segment Operation Combined with Adjunct Procedures in the Prevention of Esophagitis and Jejunitis. DAVID H. DILLARD and K. ALVIN MERENDINO, Seattle.

Canine Esophagitis After Induced Esophageal Hiatal Hernias. VINCENT GIUSEFFI, JR., JOHN H. GRINDLAY, and HERBERT W. SCHMIDT, Rochester, Minnesota.

The Influence of a Substitute Gastric Reservoir upon the Absorption of Fat and Nitrogen in Patients Who Have Had Total Gastrectomy. JOHN D. BRIGGS, JAMES A. HALSTED, and WILLIAM P. LONGMIRE, JR., Los Angeles.

The Surgical Construction of an Esophageal Valve to Replace the "Cardiac Sphincter"; an Experimental Study. DAVID H. DILLARD, CHARLES A. GRIFFITH, and K. ALVIN MERENDINO, Seattle.

A Method of Preventing Peptic Esophagitis Following Esophagogastrostomy; Experimental and Clinical Study. DAVID H. WATKINS and ARTHUR PREVEDEL, Denver.

Strangulation Obstruction; Postoperative Antibiotic Protection. ISIDORE COHN, JR., New Orleans.

Evaluation of Intestinal Absorption After Total Gastrectomy with Different Methods of Re-Establishment of Intestinal Continuity. RUDOLF O. E. OPPENHEIMER, ALBERT K. MINETA, HAROLD A. HARPER, ALLEN H. JOHNSON, FREDERIC M. BINKLEY, EDWIN E. KERR, COOPER DAVIS, and H. J. MCCORKLE, San Francisco.

Steroids

Wednesday, 9:00 a.m.—12:00 noon

Adrenal Cortical Function in Surgical Shock. DAVID M. HUME and D. H. NELSON, Bethesda.

The Influence of Alterations in Adrenal Cortical Function on the Tolerance to Trauma. ANDREW KIRSTEINS, Chicago.

Steroid Production by Incubated Human Adrenal Tissues. D. Y. COOPER, J. M. ROBERTS, and J. C. TOUCHSTONE, Philadelphia.

Adrenocortical Reserve in Debilitated Surgical Patients. EUGENE JABBOUR and JAMES D. HARDY, Memphis.

A Study of the Free 17-Hydroxy-Corticoids in the Peripheral Blood of Surgical Patients. R. W. STEENBURG, Boston.

Adrenocortical Response to Surgery in Elderly Patients. A. L. WATNE, Chicago.

Total Thyroid Gland Transplantation. JULIAN A. STERLING and RALPH GOLDSMITH, Philadelphia.

The Effect of Induced Hemorrhagic Shock on the Cerebral Circulation and Hemodynamics of Man. HRANT H. STONE, THOMAS N. MACKRELL, and PAUL NEMIR, JR., Philadelphia.

The Influence of the Addition of Sublethal Irradiation to Hemorrhage and Abdominal Injury in Dogs. JAMES W. BROOKS, RAY C. WILLIAMS, FREDERICK H. SCHMIDT, WILLIAM T. HAM, and B. W. HAYNES, JR., Richmond.

The Renal Hemodynamic Response to Hypothermia Alone and to Cross Clamping of the Thoracic Aorta With and Without Hypothermia. GEORGE C. MORRIS, JR., H. LEROY BROCKMAN, JOHN H. MOYER, and DENTON A. COOLEY, Houston.

The Use of Hypothermia in the Prevention of Neurologic Sequelae Following Temporary Occlusion of the Cerebral Circulation; an Experimental Study. ROBERT G. PONTIUS, ERIC G. HARDY, DENTON A. COOLEY, and MICHAEL E. DEBAKEY, Houston.

Experimental Production of Subcutaneous Fat Necrosis by General Hypothermia; Relation to the Chemical Composition of Fat. JESSE E. ADAMS, JOHN H. FOSTER, WALLACE H. FAULK, and H. WILLIAM SCOTT, JR., Nashville, and MACK F. STANSBURY, New Orleans.

Nutrition

Wednesday, 2:00—5:00 p.m.

Serum Lipid Levels Following Operation. CLAUDE CHOLETTE, MARY ANNE PAYNE, GEORGE N. CORNELL, and JOHN M. BEAL, New York.

An Intravenous Fat Emulsion Concentrate; Demonstration of Compatibility and Low Order of Toxicity. CHARLES BROWN, ARNOLD G. WARE, RICHARD C. SCHLANKER, and H. H. ZINSSER, Los Angeles.

Effects of Simultaneous or Previous Infusion of Sugars on the Utilization of Infused Amino Acids and Peptides. HALVOR N. CHRISTENSEN, PATRICIA BRYAN WILBER, BARBARA A. COYNE, and JOHN HERBERT FISHER, Boston.

Nutrition Studies in Surgical Patients; Preliminary Report. JOHN R. LOVELACE and JAMES D. HARDY, Memphis.

Experimental Evaluation of Prolonged Intravenous Feedings with a Mixture of Glucose, Lecithin, and Amino Acids. DONALD E. HINE and HAROLD A. HARPER, San Francisco.

Studies of Caloric, Nitrogen and Electrolyte Requirements in Decreasing Postoperative Nitrogen Loss. GEORGE N. CORNELL, HELENA GILDER, and JOHN M. BEAL, New York.

The Effect of Capillary Permeability on the Maintenance of Plasma Volume Following the Administration of Dextran and Albumin. JOHN H. DAVIS, JERREL W. BENSON, MADGE WOLFE, BURT NELSON, and WILLIAM E. ABBOTT, Cleveland.

Evaluation of a "Balanced" Amino Acid Solution for Parenteral Use. TILDEN C. EVERSON and JOHN F. LAWS, Chicago.

Hypertonic Salt Solution in Surgical Therapeusis. JAMES D. HARDY, JOHN R. LOVELACE, and HARWELL WILSON, Memphis.

Studies with Vitamin B^{12}—Co^{60}. LLOYD D. MACLEAN, Minneapolis.

A Quantitative Study of the Anatomic Distribution of Intravenous Lipid Emulsions. J. E. BEVILACQUA, G. L. KRAUSE, JR., R. E. BOTTI, and OTTO ROSENTHAL, Philadelphia.

Orthopedic Surgery

Wednesday, 2:00—5:00 p.m.

The Healing of Fractures in Experimental Animals Fed a Protein-Free Diet; Preliminary Report. JACK K. WICKSTROM, ROBERT H. HUTCHINSON, and EDWARD T. HASLAM, New Orleans.

Upper Extremity Amputation Surgery and Prosthetic Prescription. ROBERT MAZET, JR., CRAIG L. TAYLOR, and CHARLES O. BECHTOL, Los Angeles.

Freeze-Dried Arteries Used Experimentally as Tendon Sheaths. DOUGLAS R. KOTH and WILLIAM H. SEWELL, Bethesda.

Studies on Epiphyseal Stimulation. EDWARD C. PERCY and C. LAIRD WILSON, Montreal.

Experimental Study of Polyvinyl Sponge in the Formation of New Bone. A. MORGAN STRUTHERS, JOHN H. GRINDLAY, and CLYDE J. DAWE, Rochester, Minnesota.

An Experimental and Theoretical Study of Spine Stability. DONALD B. LUCAS and BORIS BRESLER, San Francisco.

The Treatment of Comminuted Fractures of the Lower End of the Radius. J. R. MOORE, Philadelphia.

A Study of Experimental Trauma to the Distal Femoral Epiphysis in Rabbits. LEE T. FORD and J. ALBERT KEY, St. Louis.

Experimental Epiphyseal Lesions in Rabbits. Z. B. FRIEDENBERG and ROBERT BRASHEAR, Philadelphia.

Excision of Ankle Joint. ANTONIO SAMSON, Montreal, Quebec.

Posterior Horn Tears of the Knee Cartilages. C. L. WILSON, Montreal.

Arthography of the Knee-Joint with Water-Soluble Contrast Medium. JEAN-PIERRE JEAN, Montreal.

Neurosurgery I

Thursday, 9:00 a.m.—12:00 noon

Brain Electrolyte Patterns in Response to Saline and ACTH. SIDNEY N. PALY and WILLIAM J. GERMAN, New Haven.

The Relief of Tic Douloureux with Stilbamidine. GEORGE W. SMITH and JOSEPH M. MILLER, Baltimore.

Partial Section of Proximal Extracranial Portion of Seventh Nerve for Facial Spasm. WILLIAM BEECHER SCOVILLE, Hartford.

Upper Alimentary Tract Ulceration and Hemorrhage Following Neurosurgical Operations. RICHARD A. DAVIS, NICHOLAS WETZEL, and LOYAL DAVIS, Chicago.

Possible Use of the Neutron Capturing Isotope Lithium^6 in the Therapy of Brain Tumors. WILLIAM H. SWEET and ALFRED J. LUESSENHOP, Boston.

Systemic Absorption and Urinary Excretion Studies of Radioactive Iodinated Albumin in the Subarachnoid Space. SHELLEY N. CHOU and LYLE A. FRENCH, Minneapolis.

Stereotaxic Placement of Radioactive Isotopes in the Brains of Laboratory Animals; a Study Oriented Toward Eventual Use in Man. JAMES B. CAMPBELL, New York.

Experimental Use of Radioactive Gold in the Subarachnoid Space. FRANK P. SMITH and F. R. PITTS, Rochester, New York.

Liver, Portacaval Anastomosis, and Other Circulatory Problems

Thursday, 9:00 a.m.—12:00 noon

Biliary Excretion of Cholesterol and Cholic Acid in the Alloxan-Diabetic Rat. W. KLATCHKO and HARRY M. VARS, Philadelphia.

The Role of the Liver in the Metabolism of Steroid Hormones in Patients with Advanced Metastatic Breast Carcinoma. M. GALANTE, J. MAX RUKES, PETER H. FORSHAM, and DAVID M. WOOD, San Francisco.

Effects of Ligation of the Inferior Vena Cava with Absorbable Ligature. FAWZI PUALWAN, GLENN E. JONES, STEPHEN BRUNY and W. ANDREW DALE, Rochester, New York.

The Role of Obstruction of the Hepatic Veins in the Pathogenesis of Ascites. JOHN M. LORÉ, JR., and JOHN L. MADDEN, New York.

Spontaneous and Induced Canine Venous Collateral Circulation After Chronic Extrahepatic Occlusion of the Portal Vein. TURLEY FARRAR, JESSE L. BOLLMAN, and JOHN H. GRINDLAY, Rochester, Minnesota.

The Pattern of Radioactive Sodium Uptake from the Colon, and its Application in Determining the Patency of a Portacaval Shunt. RALPH A. DETERLING, JR., SAMUEL POWERS, SHIVAJI BHONSLAY, and NINO MASERA, New York.

An Evaluation of Ammonia Intoxication in Normal Dogs and in Dogs Having Portacaval Anastomoses. ROBERT H. DERIEMER, DONALD E. HINE, and HAROLD A. HARPER, San Francisco.

A Method for Determining the Patency of a Portacaval Shunt. BEN EISEMAN, G. M. LINDEMAN, and J. M. JOHNSON, Denver.

Electrocardiographic Changes Following Biliary and Gastric Distention in Unanesthetized Dogs with Fresh Myocardial Infarctions. R. L. WECHSLER, A. K. KAPLAN, S. BELLET, and PAUL NEMIR, JR., Philadelphia.

The Determination of Plasma Volume and Liver Blood Flow with Rose Bengal. ARTHUR M. SIMPSON and LEO A. SAPIRSTEIN, Columbus.

Transplantation of the Liver in Dogs. EDWARD O. GOODRICH, JR., JOHN A. NELSON, T. S. BEECHER, Z. JOHN BETLEJESKI, and C. STUART WELCH, Albany.

Hepatic Blood Flow Studies in Animals with Totally Arterialized Livers. CLEM RUSS, BERNARD FISHER, JOHN HAPPEL, and ADDISON H. GIBSON, Pittsburgh.

Studies of a Drain of a Nonreactive Plastic, Teflon. FREDERICK W. PITTS and JONATHAN E. RHOADS, Philadelphia.

Plastic Surgery

Thursday, 9:00 a.m.—12:00 noon

Initial Effect of X-Ray and Grenz-Ray on Circulation as Determined by Intradermal Isotope Clearance and Transparent Chamber Observations. S. HOLMAN, E. SHAYA, F. S. HOFFMEISTER and M. T. EDGERTON, Baltimore.

Uptake of Radiothallium by Skin Graft. STEVEN P. MAGYAR, New Haven.

Tissue Banking; Cold Preservation of Skin and Use of Antifreeze Agents. JAMES E. HEMPHILL, San Francisco, JAMES BARRETT BROWN and MINOT P. FRYER, St. Louis.

The Present Status of Our Experiments with Freeze-Dried Grafts. WILLIAM H. SEWELL, DOUGLAS R. KOTH, JAMES W. PATE, and WALLACE C. BEDELL, Bethesda.

Observations on Second and Third Set Skin Homografts in the Rat. JEROME W. LEHRFELD, A. CECIL TAYLOR, and JOHN MARQUIS CONVERSE, New York.

Development of Circulation in Homologous Grafts of Skin to Recipients in Whom the Conditions Have Been Altered by Sodium Salicylate, by Histadyl, and by Irradiation. HERBERT CONWAY, RICHARD B. STARK, and JEAN SEDAR, New York.

Successful Prolongation of Survival of Homotransplants of Skin in the Rat. MELVIN E. LEVINSON and H. NECHELES, Chicago.

The Arterial Vascularization of Pedicles. HERBERT CONWAY and RICHARD B. STARK, New York.

Effect of "Pressure" Dressings Vs. "Open" Treatment on the Behavior of Grafted Third Degree Burns. S. HOLMAN, E. SHAYA, F. S. HOFFMEISTER, and M. T. EDGERTON, Baltimore.

Silicones as Subcutaneous Prostheses; Laboratory Investigations. JAMES BARRETT BROWN, MILTON LU, and MINOT P. FRYER, St. Louis.

Neurosurgery—II

Thursday, 9:00 a.m.—12:00 noon

Behavioral Effects of Electrolytic Lesions of the Periaqueductal Gray Matter in Adult Cats. F. MILES SKULTETY, RUSSELL MAYERS, and GEORGE BROWN, Iowa City.

Continuous Cervical Sympathetic Block. ALBERT FIELDS, Los Angeles.

Surgical Approach to Pituitary Stalk Section in Dogs. ALAN B. ROTHBALLER, STANLEY C. SKORYNA, and DONALD R. WEBSTER, Montreal.

Brain Changes Associated with Air Embolism. C. C. FRIES, K. E. KARLSON, S. ADLER, B. LEVOWITZ, A. COOK, and CLARENCE DENNIS, Brooklyn.

Neurophysiological and Pathological Findings Following Acute Occlusion of an Anterior Choroidal Artery in Man. ROBERT W. RAND, W. EUGENE STERN, and W. JANN BROWN, Los Angeles.

Experimental Homologous Dura Preserved by Freeze-Drying for Repairing Dural Defects. WILLIAM H. SEWELL and DOUGLAS R. KOTH, Bethesda.

Experimental Concussion. Relation of Physiological Effect to Time Duration of Increase in Intracranial Pressure at the Time of Impact. H. R. LISSNER, B. F. HADDAD, and F. R. LATIMER, Detroit.

Observations on Ventricular and Lumbar Subarachnoid Peritoneal Shunts in Hydrocephalus in Infants. MICHAEL SCOTT, HENRY T. WYCIS, FREDERIC MURTAGH, and VICTOR REYES, Philadelphia.

FUTURE CLINICAL CONGRESSES

1955	Chicago, Illinois	October 31 to November 4
1956	San Francisco	October 8 to 12
1957	New York or Atlantic City	September or October

THE CLINICAL CONGRESS TECHNICAL EXHIBITION

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Abbott Laboratories	314, 316
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American Hospital Supply Corporation	306, 308
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John F. Greer Company	525
Grune & Stratton, Inc.	140
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